“FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS AND MANAGEMENT OF THYROID DISEASES”

Dissertation submitted in partial fulfillment of the Requirement for the award of the degree of

MS DEGREE EXAMINATION

GENERAL SURGERY

Tirunelveli

DEPARTMENT OF GENERAL SURGERY

TIRUNELVELI MEDICAL COLLEGE

THE TAMILNADUDR.MGR MEDICAL UNIVERSITY

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April 2014

CERTIFICATE

This is to certify that the dissertation titled "**FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS AND MANAGEMENT OF THYROID DISEASES"**is the original work done by Dr.Anit Joseph K,Post Graduate in Dept. Of General Surgery,Tirunelveli,to be submitted to the Dr.MGR Medical University Chennai-32 towards the partial fulfillment of the requirement for the award of MS Degree in General surgery April 2014.

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LIST OF ABBREVIATIONS USED

AntiTG	-	Antithyroglobulin
AntiTPO	-	Anti thyroid peroxidase
ATD	-	Antithyroid drugs
BMR	-	Basal metabolic rate
Cm	-	centimeter
CT	-	Computerised tomography
DIT	-	Di iodo tyrosine
ECG	-	Electrocardiogram
ESR	-	Erythrocyte sedimentation rate
FNA	-	Fine needle aspiration
FNAB	-	Fine needle aspiration biopsy
FNAC	-	Fine needle aspiration cytology
FTI	-	Free thyroxine index
G	-	Gauge
H&E	-	Hematoxylin and eosin
HLA	-	Human Leucocyte Antigen
HPE	-	Histopathological examination
HT	-	Hemithyroidectomy

I_{123}

I_{125} } Radioactive isotopes of iodine

I_{130}

I_{131}

LATS	-	Long acting thyroid stimulation
mC i	-	milli curie
mg	-	milligram
MIT	-	Mono iodo tyrosine
MNG	-	Multi nodular goiter
MRI	-	Magnetic resonance imaging
PBI	-	Protein bound iodine
RLN	-	Recurrent laryngeal nerve
rT_3	-	reverse tri iodothyronione
T_3	-	Tri iodothyronine
T_4	-	Thyroxine
TAA	-	Thyroid auto antibodies
TBG	-	Thyroxine binding globulin
TBPA	-	Thyroxin binding prealbumin
Tc	-	Technetium
TRH	-	Thyrotropin releasing hormone
TSH	-	Thyroid stimulating hormone
USG	-	Ultrasonography

ABSTRACT

Background and Objectives

Swellings of thyroid are frequently encountered in surgical practice. Clinical evaluation helps in early diagnosis but its difficult to distinguish early malignant lesions from the most prevalent benign goiters.A variety of tests has been employed to distinguish between benign from malignant thyroid nodules. A radionucleotide scan with Radioiodine or Technetium helps in diagnosis but doesnot provide an accurate histological diagnosis. USG can differentiate between only solid and cystic swellings. Surgical excision is the only means by which a definitive diagnosis is obtained based on HPE. An alternative approach is called for other than surgery as most cases are benign. FNAC is a simpler and safer procedure carried out in the OPD with minimum equipment and it also has a good patient compliance. The present study aims at correlating the cytological diagnosis with the final histological diagnosis to evaluate the sensitivity, specificity and accuracy of FNAC smears, thereby its role in preoperative diagnosis in planning proper management.

Methodology

A proforma was drafted for the study of all patients presenting with history of palpable thyroid swelling and undergo surgery in our hospital. Clinical presentations, FNAC and histopathology of all cases were documented. Only those patients, whose specimen contained adequate material were included in the study.

Results

100 cases who presented with thyroid swellings were studied and their histopathological diagnosis was compared with the FNAC. Out of the 100 cases, 88 were females and 12 were males, being 7.3 : 1. Of the 86 cases which were seen benign by FNAC, 82 were confirmed by histopathology. Of the 18 cases which were proved to be malignant by histopathology 14 were only seen as malignant by FNAC. The sensitivity of FNAC in the diagnosis of benign lesions was found to be 77.78% , specificity was 100%, positive predictive value 100% and accuracy is 96%.

Interpretation and Conclusion

The majority of our patients were between second and third decade, of which females being predominant. The majority of cases were benign of which multinodular goiter being the most dominant pathology (25 %). Among the malignancies, majority being papillary carcinoma (78.94 %).The sensitivity, specificity and predictive value of positive smears being 77.78%, 100 %, and 100% respectively. FNAC was of greater help in the preoperative management of thyroid swellings. Multinodular goiters and colloid goiters were distinguished easily by FNAC but confusion prevailed in cases of follicular adenomas. Majority of our patients were rural folks, who cannot be followed up regularly and for a longer time, so clinical suspicion should be one of the indications for surgery, inspite of FNAC being negative. FNAC is simpler, safer, quicker and

more informative, when compared with other sophisticated methods in the diagnosis of thyroid lesions.

KEYWORDS : Fine needle aspiration cytology; Thyroid swelling; accuracy; positive predictive value.

INTRODUCTION

Thyroid diseases are among the commonest endocrine disorders worldwide.Majority of these are benign diseases of which goiter is the commonest and a few are malignant. India too, is no exception. The magnitude of problem in South East Asia is estimated to be around 172 million with goiters and iodine deficiency is estimated to be around 600 million. It has been estimated that about 42 million people in India suffer from thyroid diseases**.** Thyroid nodules are common clinical findings and have a reported prevalence of 4% to 7% in the adult population. Discrete thyroid swellings are common and are present in 3-4% population in UK and USA. Thyroid swellings are four times more common in females. The incidence increases with age, a history of radiation exposure and diet containing goitrogens. Thyroid swellings can be isolated or dominant. True incidence of thyroid nodularity is less apparent on clinical classification. When such glands are exposed at operation, clinically impalpable nodules are often detected. The usual presentation of thyroid disease is with swelling, pressure symptoms or signs of toxicity. Importance of discrete thyroid nodule lies in the risk of neoplasia as compared to other thyroid swellings. Fifteen percent of isolated swellings are malignant. The vast majority of these nodules are non neoplastic lesions or benign neoplasms. However, the distinction of these benign lesions from a malignant nodule cannot be based

reliably on the clinical presentation alone. Complications of surgery are possible injury to the recurrent laryngeal nerve, hypoparathyroidism and thyroid hormone dependence. The available tools to know the nature of a thyroid nodule are thyroid function tests, thyroid antibody titers, isotope scans, ultrasonography and fine needle aspiration cytology. Several diagnostic tests such as scintigraphy (with I^{123} or ^{99m}TC pertechnetate), ultrasonography and fine needle aspiration cytology (FNAC) have been used to differentiate benign from malignant thyroiddisease pre operatively. FNAC has now supplanted most of the other tests forpre-operative evaluation of thyroid nodules.Due to its simplicity, low cost and absence of major complications, thisprocedure is being performed on an increasing number of patients, which has ledto the detection of thyroid cancers at earlier stages, resulting in better outcome ofpatients.

FNAC is an integral part of selected patient management but comprisesonly part of overall evaluation. FNAC is usually performed in clinicallypalpable nodules. If nodules are not palpable, then this procedure can beperformed under ultrasound guidance. Overall diagnostic efficacy of FNACis 94.2%. However, only limitation is to differentiate betweenfollicular adenomaand carcinoma. Major load of unnecessary surgery can be avoided by perfectionand routine use of FNAC in solitary thyroid nodules. FNAC is a simple and costeffective biopsy technique that can be performed on out-patient basis.Practice guidelines set forth by the American Thyroid

Association andNational Comprehensive Cancer Network state that FNA should be used as theinitial diagnostic test because of its superior diagnostic reliability and costeffectiveness before both thyroid scintigraphy and ultrasonography.Although several studies have been done to prove the efficacy of FNACin diagnosing thyroid swelling, the sensitivity of studies done to assess theefficacy of FNAC ranges from 65% to 98% and specificity ranges 72% to100%.Nevertheless, like any other test FNAC has its limitations. The reportedpitfalls are those related to specimen adequacy, sampling techniques, the skill ofthe physician performing the aspiration, the experience of the pathologistinterpreting the aspirate and overlapping cytological features between benign andmalignant follicular neoplasm. Because of this discrepancy in the result, the present study wasundertaken to assess the accuracy of Fine needle aspiration cytology in patientspresenting with thyroid swelling.

AIM OF THE STUDY

The aim of the study is to determine the accuracy and the role of fine needle aspiration cytology (FNAC) as a diagnostic modality in the diagnosis and treatment of thyroid diseases.

OBJECTIVES

1. To determine the role of FNAC in the diagnosis and management of thyroid disorders.
2. To evaluate the efficacy and accuracy of FNAC in diagnosis of thyroid disorders.
3. To determine the cost effectiveness of FNAC in the preoperative diagnosis of thyroid disorders.
4. The diagnosis of diffuse non toxic goiter, in distinguising between colloid goitre and auto immune thyroiditis.
5. In distinguising between the malignant and benign solitary nodular lesions and recurrent goiters thereby reducing the cost of unnecessary surgery for a benign lesion.
6. In confirming the clinically obvious malignancy of thyroid thereby determining the type of surgery.
7. To obtain material for special laboratory investigations aimed at the prognosis of thyroid diseases.

REVIEW OF LITERATURE

Historical aspects

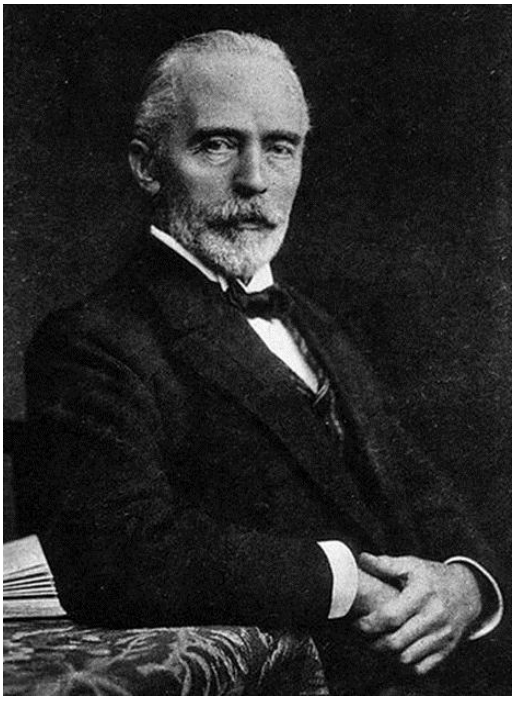
The thyroid gland was previously referred to as the laryngeal gland and was subsequently named thyroid by Wharton in 1645. Existence of thyroid gland was known to Galen (2 A.D), who thought that it provided fluid for lubrication of the larynx. Sir Astley Cooper (1768-1841) said it has a function of secretion. Thyroxine (T_4) was isolated by Kendall in 1965 and it was synthesized by Harrington and Banger in 1927. In 1953 the important discovery of 3, 5, 3 Tri-iodothyronine was made by Cross and Pitt-rivers and also by Roche, Liesitsky and Michel simultaneously. The introduction of radioactive iodine in 1934, made it possible for the clear understanding of thyroid physiology. The term thyroid gland (*Greek thyreoeides, shield shaped*), is attributed to Thomson Wharton in his Adenographia (1656). Thyroid was classified as a ductless gland by Albrecht von Haller in 1776.

EARLY OPERATIONS

The first credible account of thyroid surgery was given, by Roger Frugardi of Salerno in 1170.The first well-documented partialthyroidectomy was undertaken in Parisin 1791 by Pierre Joseph Desault (1744-1795).By the 19th century, the advent of general anaesthesia(1840's), antisepsis (1860's) and haemostasis (1870's), enabled surgeons toundertake more thyroid operations, with greatly reducedmortality. Between 1850 and 1977, the world

wide operative mortality fell toaround 20%.The leading thyroid surgeons at this time were Theodor Kocher (1841-1917) and Theodor Billroth (1829-1894). Both of them performed thousands ofthyroidectomies, with increasingly successful results. Kocher discovered that total thyroidectomy wasfollowed by development of myxoedema and he demonstrated that thiscomplication could be prevented by subtotal thyroidectomy. Kocher was awardedNobel Prize in 1909 in recognition ‘for his works on the physiology,pathology and surgery on thyroid glands’.Theoder Kocher is regarded as father of thyroid surgery.

Fig. 1 .



EMIL THEODOR KOCHER (1841-1917)

Embryology

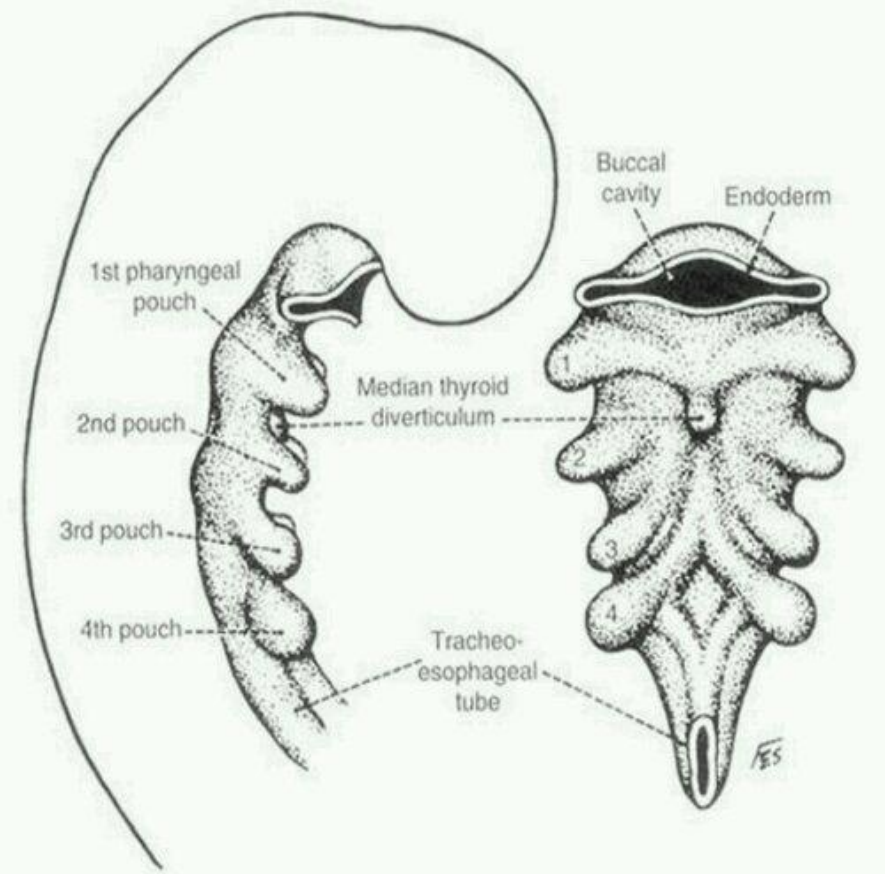


Fig. 2 . Thyroid embryology

The thyroid arises as an outpouching of the primitive foregut around third week of gestation. It originates at the base of tongue at the foramen caecum. Endodermal cells at the pharyngeal anlage thicken to form the medial thyroid anlage that desends in the neck anterior to structures that form the hyoid bone and larynx. During its descend the thyroid anlage is connected to the foramen caecum through an epithelial-lined tube known as thyroglossalduct. The epithelial cells making up the anlge give rise to thyroid follicular cells. The paired anlages arising from the fourth branchial pouch fuse with the median

anlage at around fifth week of gestation. The lateral anlages are neuroectodermal in origin (ultimobranchial bodies),they provide the calcitonin producing parafollicular cells or C cells, which lies in the superoposterior portion of the gland. Thyroid follicles are initially apparent by 8th week and colloid formation begins by 11th week of gestation.

Surgical anatomy

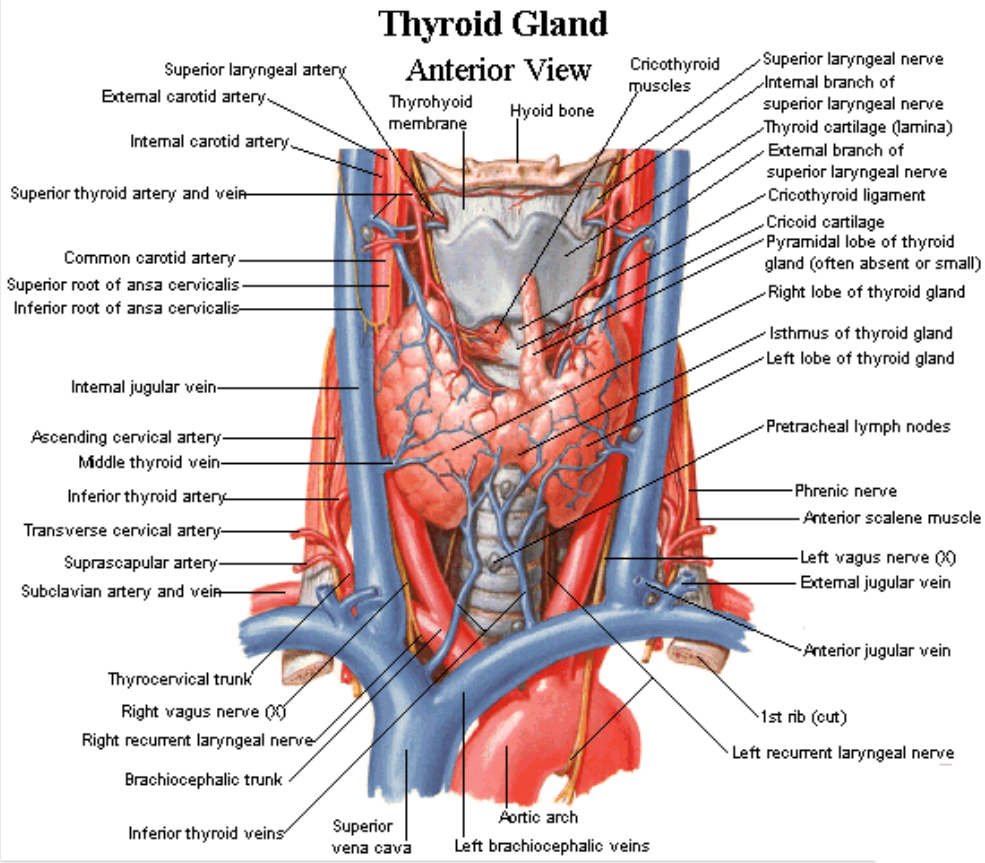


Figure 3. Thyroid gland, anterior view

The adult thyroid gland is brownish-redin colour located anteriorly inthe lower neck, extending from the level of the fifth cervical vertebra down to thefirst thoracic, overlying the second to fourthtracheal rings.

Although thyroid weight varies, it averages 20 gm in adults (it is slightlyheavier in women). Thyroid glands are located adjacent to thyroidcartilage, and isthmus is located just below the cricoid cartilage.A pyramidal lobe is seen in about 50% of patients. Usually, two pairs of parathyroid glands lie in proximity to thethyroid gland.

Innervation of the thyroid

Principal innervation of the thyroid gland is derived from theautonomicnervous system. Parasympathetic fibers come from the vagus nerves, andsympathetic fibers are distributed from the superior, middle, and inferior gangliaof the sympathetic trunk. These small nerves enter the glandalong with the bloodvessels. Autonomic nervous regulation of theglandular secretion is not clearlyunderstood, but most of the effect is postulated to be on blood vessels, hence theperfusion rates of the glands.

Fascia and Ligament

The thyroid gland is ensheathed by the visceral fascia, a division of themiddle layer of deep cervical fascia, which attaches it firmly to thelaryngoskeleton. The anterior suspensory ligament extends from the superiomedialaspect of each thyroid lobe to the cricoid and thyroid cartilage. Theposteromedial aspect of the gland is attached to the side of the cricoid cartilage,first and second tracheal ring, by the posterior suspensory ligament

(Berry'sligament). This firm attachment of the gland to the laryngoskeleton is responsiblefor movement of the thyroid gland and related structures during swallowing.On its way to the larynx, the recurrent laryngeal nerve usually passes deepto the Berry ligament or between the main ligament and its lateral leaf. Deep tothe ligament, but lateral to the nerve, is a posteromedial portion of the thyroidlobe, which may be overlooked during thyroidectomy.

Strap Muscles

The lateral surface of the thyroid is covered by the sternothyroid muscle,and its attachment to the oblique line of the thyroid cartilage prevents the superiorpole from extending superiorly under the thyrohyoid muscle. More anteriorly arethe sternohyoid and superior belly of the omohyoid muscle, overlapped inferiorlyby the anterior border of the sternocleidomastoid muscle. The sternohyoid andsternothyroid muscles are joined in the midline by an avascular fascia that mustbe incised to retract the strap muscle laterally in order to access the thyroid glandduring thyroidectomy. If strap muscles are to be transected for better exposure,do so high in the neck, because the motor nerve supply from the ansacervicalisenters these muscles inferiorly.

Vascular Anatomy

The arterial supply to the thyroid gland comes from the superior andinferior thyroid arteries and, occasionally, from the thyroidima. The

thyroid ima is a single vessel that, when present, originatesfrom the aortic arch or the innominate artery and enters the thyroid gland at theinferior border of the isthmus.The superior thyroid artery is the first anterior branch of the externalcarotid artery. In rare cases, it may arise from the common carotid artery justbefore its bifurcation. The superior thyroid artery descends laterally to the larynxunder the cover of the omohyoid and sternohyoid muscles. The artery runssuperficially on the anterior border of the lateral lobe, sending a branch deep intothe gland before curving toward the isthmus, where it anastomoses with thecontralateral artery.Cephalad to the superior pole, the external branch of the superiorlaryngeal nerve runs with the superior thyroid artery before turning medially tosupply the cricothyroid muscle. The inferior thyroid artery arises from the thyrocervical trunk, a branch ofthe subclavian artery. It ascends vertically and then curves medially to enter thetracheoesophageal groove in a plane posterior to the carotid sheath. Most of itsbranches penetrate the posterior aspect of the lateral lobe.

The inferior thyroid artery has a variable branching pattern and is closelyassociated with the recurrent laryngeal nerve. The latter also ascends in thetracheoesophageal groove.

Venous Drainage

Three pairs of veins provide venous drainage for the thyroid gland. Thesuperior thyroid vein ascends along the superior thyroid artery and

becomesatributary of the internal jugular vein. The middle thyroid vein follows a directcourse laterally to the internal jugular vein. The inferior thyroid veins followdifferent paths on each side. The right passes anterior to the innominate artery tothe right brachiocephalic vein or anterior to the trachea to the left brachiocephalicvein. On the left side, drainage is to the left brachiocephalic vein. Occasionally,both inferior veins form a common trunk called the thyroid ima vein, whichempties into the left brachiocephalic vein.

NEVRE SUPPLY

The left recurrent laryngeal nervearises from the vagus nerve at the crossing of aortic arch and loops aroundligamentumarteriosum and ascends medially in the neck within the tracheoesophaeal groove. The right recurrent laryngeal nerve arises from the vagus where it crosses the right subclavian artery.The relationship between the nerve and the inferior thyroid artery ishighly variable, as demonstrated by the classic work of Reed, who in 1943described 28 variations in this relationship. The nerve can be found deep to theinferior thyroid artery (40%), superficially (20%), or between branches of theartery (35%). Significantly, the relationship between nerve and artery on oneside of the neck is similar to that found on the other side in only 17% of thepopulation. Furthermore, at the level of the inferior thyroid artery, branches of therecurrent laryngeal nerve that are extralaryngeal may be present (5%).Preservation of all of those branches is important during

thyroidectomy.Another hint to the location of the recurrent laryngeal nerve is theZuckerkandl tubercle, an extension of the thyroid, which is close to the Berryligament.

On rare occasions, the recurrent laryngeal nerve may be nonrecurrent as seen in 0.5 to 1 % of patients, may pass directlyfrom the vagus to the larynx, close to the superior thyroid vessels. This formationis nearly always observed on the right side and is associated with aretroesophagealsubclavian artery. However, the formation can occur on the leftside in cases of transposition of the great vessel, the RLNs terminate by entering the larynx posterior to cricothyroid muscle. The RLNs innervte all the muscles of larynx except the cricothyroids, which are innervated by the external laryngeal nerves.

Injury to one RLN leads to paralysis of one vocal cord which comes to lie in the paramedian or abducted position. The paramedian position leads to a weak voice but abducted position leads to hoarse voice and an ineffective cough. Bilateral RLN injury leads to airway obstruction which may necessitate tracheostomy or loss of voice.

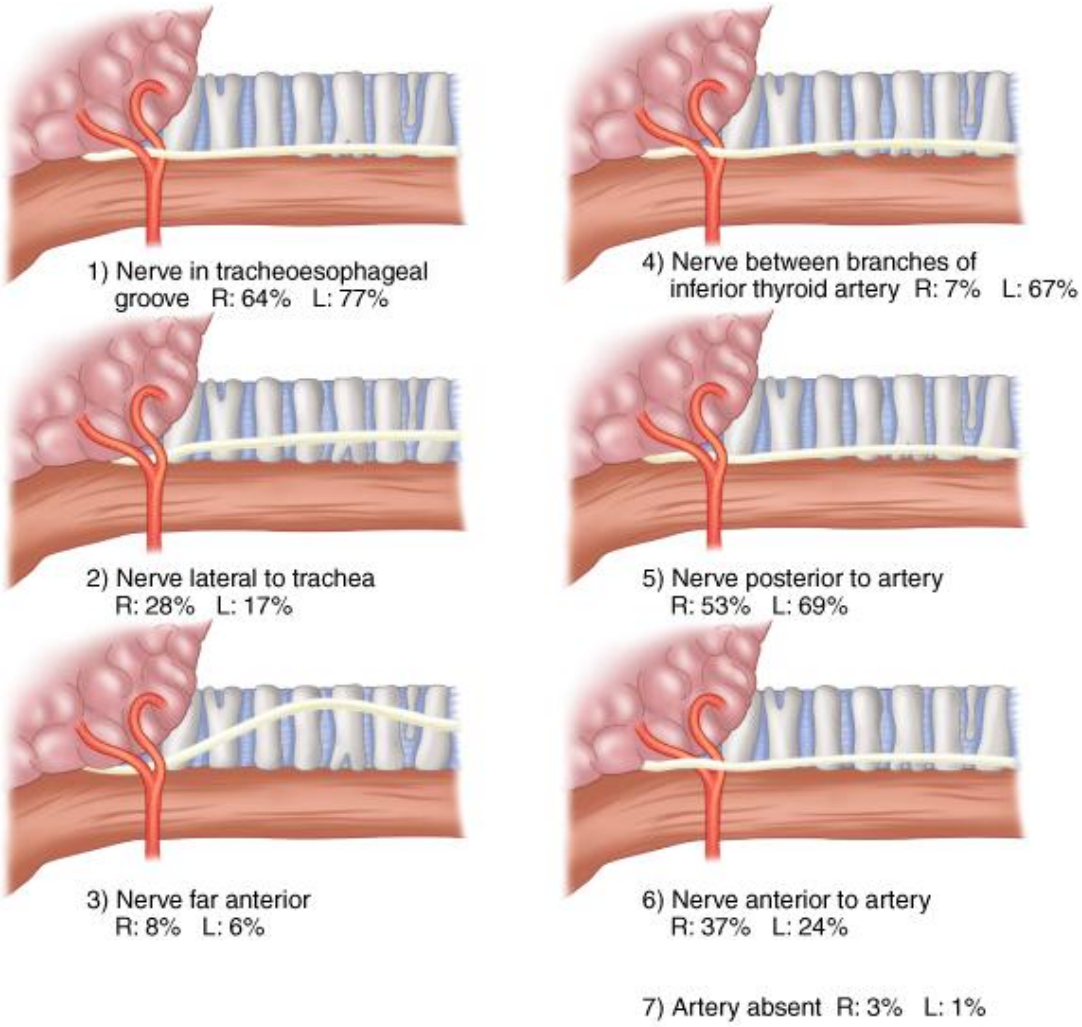


Fig .4 : **Recurrent laryngeal nerve**

The superior laryngeal nerves also arise from the vagus nerve and travel along internal carotid artery. The internal branch is sensory to thesupraglottic region and the external branchlies on the inferior pharyngeal constrictor muscle and descends along with the superior thyroid vessels to innervate the cricothyroid.

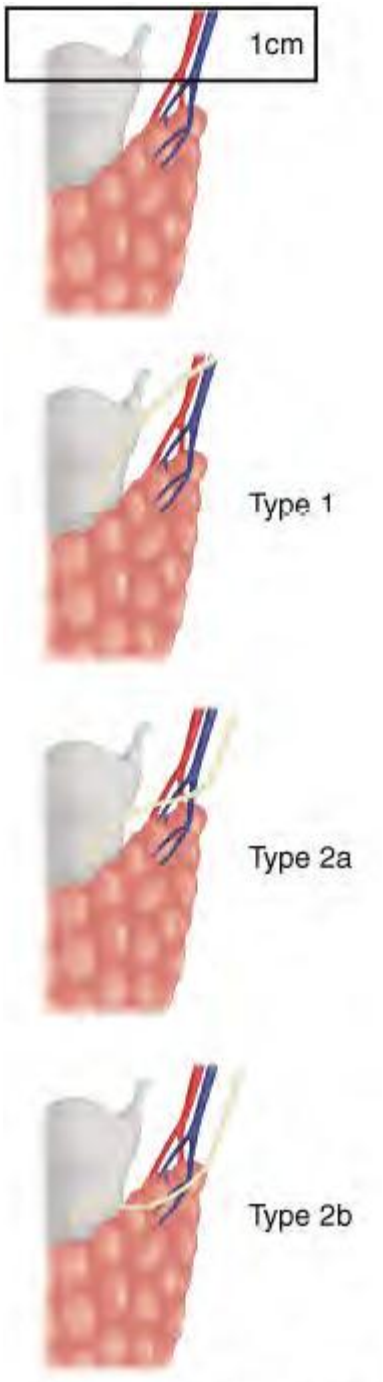


Fig. 5 : Relationship of recurrent laryngeal nerve to superior thyroid vessels

Cernea and collegues proposed a classification system to describe relationship of this nerve to the superior thyroid vessels.

In type 1 anatomy the nerve crosses ≥ 1cm above the superior thyroid pole.

In type 2 nerve crosses <1 cm above the superior thyroid pole.Type 2a variant, in which nerve crosses below the tip of the superior pole of thyroid,occurs in 20% of individuals which places the nerve at risk of injury during thyroidectomy.

High ligation of the superior thyroid artery during thyroidectomy places this nerve at risk of inadvertent injury, which would produce difficulty " hitting high tones", projecting the voice, and voice fatigue during prolonged speech.

Lymphatics

Lymphatic drainage of the thyroid gland is extensive and flowsmultidirectionally.Intraglandular lymphatic vessels connect both thyroid lobes through the isthmus and also drain to perithyroid structures and lymph nodes. Regional lymph nodes include pretracheal, and paratracheal, periglandular nodes; to the prelaryngeal (Delphian), nodes along the recurrent laryngeal nerve; retrophayngeal, esophageal, and superior mediastinal,upper,middle and lower jugular lymph nodes. There can also be "skip" metastasis to nodes in the ipsilateral neck.

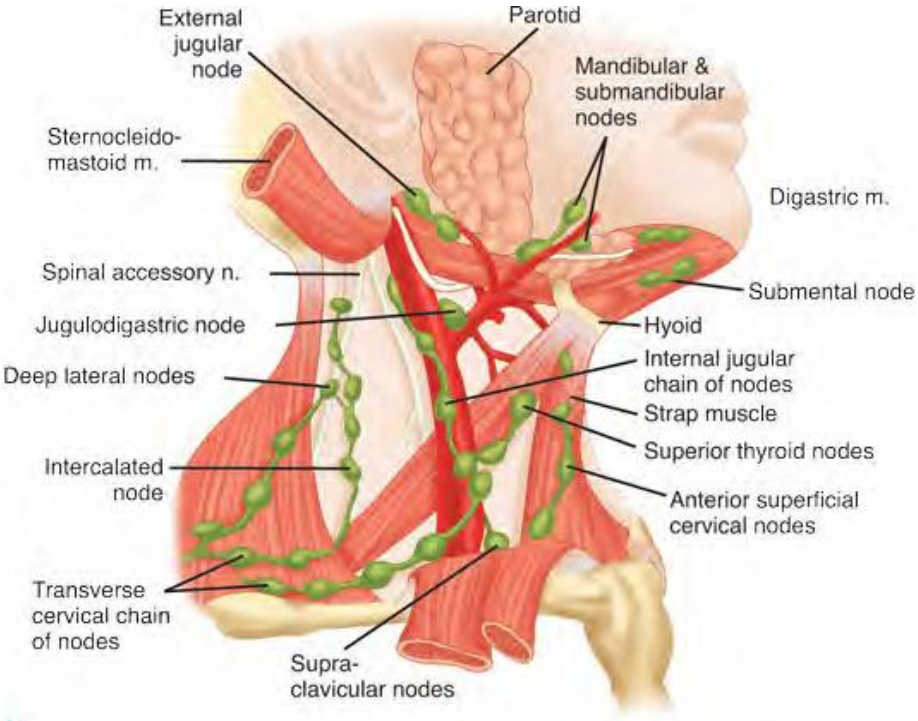


Fig .6 :Lymphatics 1

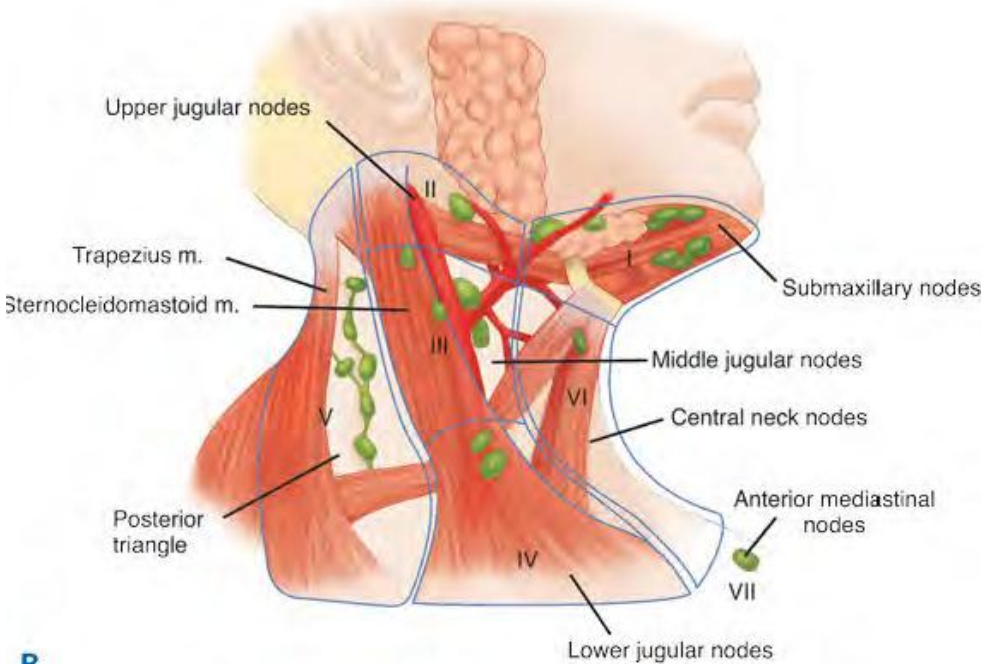


Fig .7 :Lymphatics 2

Structure

Under the middle layer of deep cervical fascia, the thyroid has an innertrue capsule, which is thin and adheres closely to the gland. Extensions of thiscapsule within the substance of the gland form numerous septae, which divide itinto lobes and lobules. The lobules are composed of follicles, which forms the structural unitof the gland. They are 200-900 microns in diameter. The follicle is lined by a single layer of cells varying from flattened to cuboidal in shape depending on activity, enclosing a colloidfilledcavity.

The colloid (pink on hematoxylin and eosin) contains an iodinated glycoprotein, iodothyroglobulin, a precursor of thyroid hormones. Epithelial cells are of 2 types: principal cells (follicular) and parafollicularcells (C, clear, light cells). Principal cells are responsible for formation of thecolloid (iodothyroglobulin), whereas parafollicular cells produce the hormonecalcitonin, a protein central to calcium homeostasis. Parafollicular cells lieadjacent to the follicles within the basal lamina. They stain with agryophil silver stain or immunohistochemicalmethods.

Hurtle cells are follicular cells with abundant granular acidophilic cytoplasm. The fibrous tissue stroma between the follicles are penetrated by blood vessels, nerves and lymphatics with lymphocytic aggregations.

Cytology of normal thyroid gland

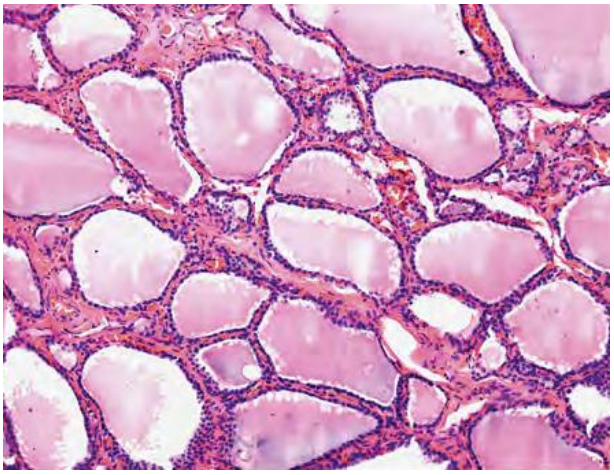


Fig. 8 : **Normal thyroid histology- Follicular cells surround colloid**

The follicles are rarely extracted intact in aspiration of thyroid. Usually fragments of follicles are observed,the cells are arranged in small clumps and sheets. Nuclei are round to oval with definite borders. Distinct nucleoli are rarely found. Cytoplasm stains greyish violet with Giemsa stain whereas tan with Papanicolaou stain. Colloid appears pink or orange yellow. Cell borders are indistinct or is feathery. Granular cytoplasm is seen occasionally.The characteristic feature of this cell is that they are uniform cells with fragile,partially dispersed cytoplasm,bare nuclei in a background of thin colloid.

Physiology

The primary function of thyroid gland is the production of sufficientthyroid hormones for proper regulation of cellular metabolism throughout thebody. The thyroid hormones triiodothyronine (T_3) and L-

thyroxine (T_4) {extracted by Kendall EC in 1953} are bound to thyroglobulin in the colloid.

Iodine metabolism

Iodine is taken in the form of Iodides. Sea fish,egg and milk are gooddietary source of iodide. Dietary iodide is absorbed from upper gastrointestinaltract and carried as inorganic iodide in plasma. Normally thyroid, salivary glandsand kidney compete for iodide but thyroid and kidney are the principal organsthat compete for iodide.

The adult man requires 0.14 mg of iodide per day and an adult femalerequires 0.10 mg. Growing children, pregnant and lactating women require more.The daily requirement is met by balanced diet and drinking water, exceptionbeing hilly areas where food and water may be deficient in iodine.

Synthesis, secretion and transport of thyroid hormones

The synthesis of thyroid hormones is divided into four steps:

Iodine trapping

The thyroid traps the plasma iodine in the inorganic form. It is essentially an active process, involving ATP dependent transport across the basement membrane via an intrinsic membrane protein, the sodium/iodine (Na+/I-) symporter and stimulated by TSH. It is competitively inhibited by Thiocynates and Perchlorates.

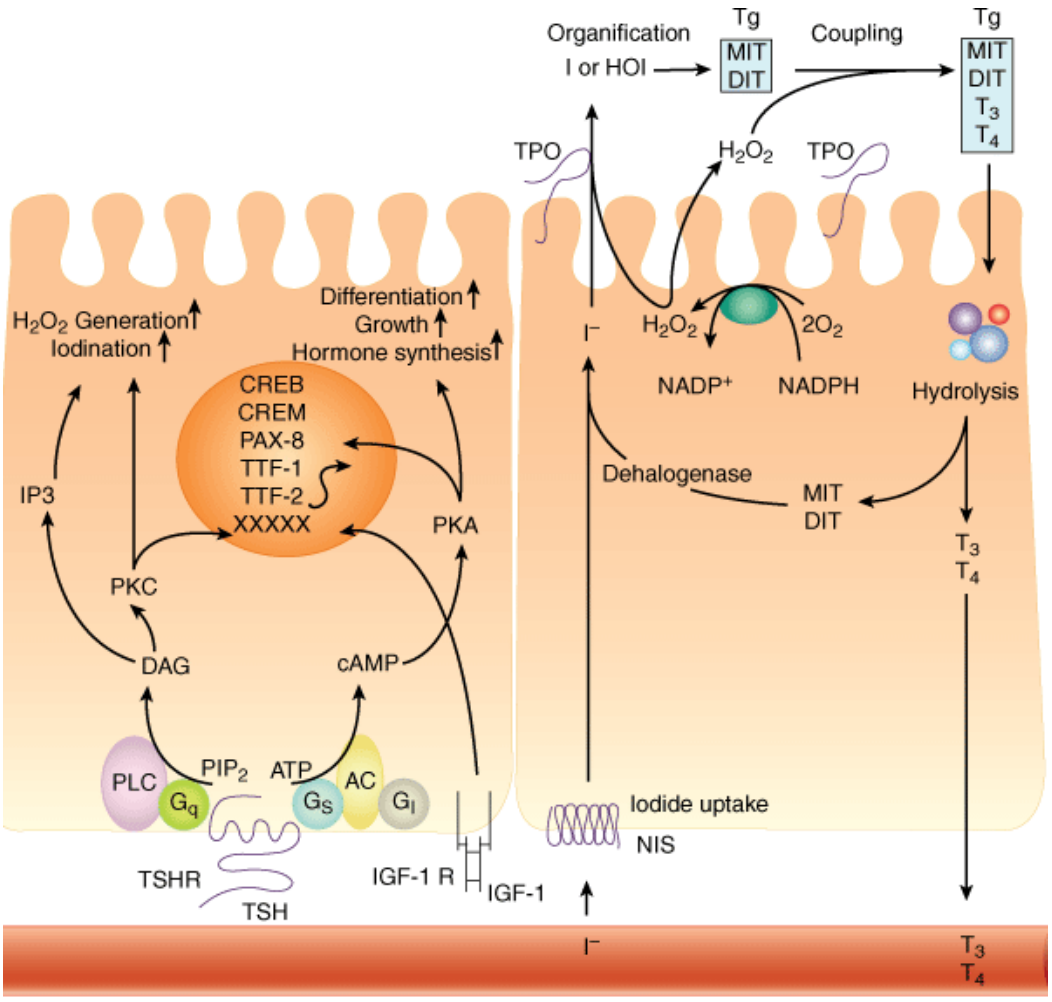


Fig.9 : Synthesis, secretion and transport of thyroid hormones

Iodine binding

The inorganic iodide is oxidized to inorganic iodine at the thyroidfollicular cells with the help of an enzyme peroxidase. Iodine combines withamino acid tyrosine in the globulin molecule within the follicular cells to form monoiodotyrosine and diiodotyrosine (MIT and DIT), process is inhibited byThiouracil group of antithyroid drugs and by PAS and chloroquine. A recently identified protein pendrin,is thought to mediate iodine efflux to the apical membrane.

Coupling

Thyroxine (T_4) is formed by coupling of two molecules of DIT, andTriiodothyronine (T_3) by coupling of one molecule of each MIT and DIT. Thecoupling reaction occurs at the Thyroglobulin molecule. They are oxidativereactions and need peroxidase enzyme.

Hormonal release

Thyroglobulin is first taken up by thyroid follicular cells. Under the influence of TSH a protease acts on thyroglobulin to release T_4, T_3, MIT and DIT. MIT and DIT are de-iodinated within the cell and iodine is reutilized for iodinating globulin. From the follicular cells T_4 and T_3 directly enters thecirculation. On entering the circulation the thyroid hormones are largely bound tospecific protein called thyroxine-binding globulin (TBG), thyroxine bindingalbumin and thyroxine binding prealbumin (TBPA).This protein has got more affinity to Thyroxine than to the triiodothyronine.The protein bound iodine (PBI), which is about 4-8 g per 100 mlmainly, reflects plasma T_4 level. A small amount of hormone remains free in theserum in equilibrium with the protein bound hormone and is biologically active.

The free hormone is physiologically active and protein bound fraction acts as areserve. Thyroid hormones are disposed by de-iodination in 80% and 20% is excretedin the stools.

Ineuthyroid state, most of the hormone produced is of T_4 and only 20% of T_3 is produced. Most of the T_3 is produced by the conversion of T_4 to T_3 in the liver,muscles,kidneyand anterior pituitary by the action of the enzyme 5' -mono- deiodinase.About 40% of circulating T4 is converted to T_3 peripherally called"Reverse T_3". This is inhibited by propranolol and glucocorticoids.

Differences between T3 and T4

T_3 has quicker onset of action and is effective in very small doses. Its three to four times more active than T_4 per unit weight. Theonset of action of T_3 is within 6-8 hours and that of T_4 is 4-14 days. Aftercessation of therapy the hormonal effect lasts for several days with T_4 butvanishes quickly with T_3.The half life of T_3 is 1 day when compred to T_4 which is 7 days. T_3 is the more important physiological hormone and isalso produced in the periphery by conversion from T_4. Reverse T_3 is an inactiveform of T_3.

Regulation of thyroid function

Thyroid function is regulated by two mechanisms, namelysuprathyroidand intrathyroid. The suprathyroid regulation is by thyroid stimulating hormone(TSH) released from basophilic cells of the anterior pituitary. TSH stimulatesthyroid hypertrophy and hyperplasia. All steps in the synthesis and secretion ofthyroid hormones are enhanced and the synthesis of thyroglobulin is increased.

These actions of TSH are due to binding of hormone to receptors on thyroidfollicular cell membrane. Regulation of TSH secretion is by two opposingmechanisms.

The thyrotrophic-releasing hormone (TRH) of hypothalamic originstimulates synthesis and secretion of TSH and thyroid hormones. TRH issynthesized in the hypothalamus, reaches anterior pituitary by portal bloodsystem and binds to receptor on thyrotrophic cells. This is called pituitary –thyroid axis. The intrathyroidal regulation is also called autoregulatorymechanism, but this is not to mean that thyroid controls hormone production inthe absence of TSH stimulation. The gland reduces the iodine trappingmechanism whenever there is sudden increase in the supply of iodide and thisoccurs without the negative feedback mechanism.

Thyroid stimulating antibodies

A family of IgGimmunoglobulins bind with TSH receptor sites (TRAbs)and activate TSH receptors on the follicular cell membrane. They have a moreprotracted action than TSH (16-24 hours versus 1.5-3 hours) and are responsiblefor virtually all cases of thyrotoxicosis not due to autonomous toxic nodules.

Serum concentrations are very low and not routinely measured.

Etiology of benign disorder

Simple goiter develop as a result of stimulation of thyroid gland by TSH,either as a result of inappropriate seretion from microadenomin the anterior pituitary (which is rare) or in response to a chronically low level of circulating thyroid hormones.defetive synthesis of thyroid hormones also produes some sporadic goiters.

(a) Iodine deficiency

The daily iodine requirement is about 0.1 to 0.15 mg. In nearly all cases where simple goiter is endemic,there is very low iodine content in food and water. However in situations where iodine excess occurs,disease processes suh as Hashimoto's thyroiditisand Grave's disease can occur.

(b) Chemical goitrogens

Iodides in large quantities are goitrogenic as they can inhibit organic binding of iodine and produce an iodide goiter (Wolf – Chaikoff effect).

(c) Drugs as goitrogens

The vegetables of Brassica family (cabbage,kale and rape) contain thiocynate and drugs like PAS (para-amino salicylic acid) and anti thyroid drugs are goitrogens.

Thiocynates and perchlorates interfere with iodine trapping, carbimazole and thiouracil compounds interfere with oxidation of iodide and binding of tyrosine. Massie steroid therapy may result in functional hypothyroidism.

(d) Genetics and immuniology

Grave's disease is associated with Human Leucocyte Antigen (HLA) halotypes – HLA-B^8, HLA- DR^3 and HLA – DQAI. The hypertrophy and hyperplasia is attributed to abnormal thyroid stimulating antibodies (TSH-RAb) that bind to TSH receptor sites and produce a disproportionate and prolonged effect.

Etiology of malignancy

(a) Radiation

Papillary carcinoma is associated with irradiation of thyroid gland below 5 yr of age. Men age at presentation is 30 to 40 yrs. Patients who have received external radiation for soft tissue malignancy like Hogdkin's lymphoma are at increased risk of developing malignancy.

(b) Raised TSH levels

The incidence of follicular carcinoma is high in endemic goitrous areas, may be due to TSH stimulation.

(c) Genetic predisposition

Sporadic and familial medullary and follicular carcinomas are associated with RET oncogen mutation.RET/PTCB is associated with short latency aggressive papillary carinoma. P^{53} mutation is associated with undifferentiated thyroid cancer and thyroid cancer cell lines. PAX ^{8} gene is found to have an important role in follicular neoplasms, including follicular carcinomas.

HISTORY AND EVOLUTION OF FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

HISTORICAL ASPECTS

Cytology has its roots from the time of Virchow(1821 – 1901) and Von Gerllac(1958). It was pioneered by Beale (1906), Dudgeon and Ptrick (1927), Dudgeon and Barott (1934), Mrtis and Ellis (1930 and 1934) , Dudgeon and Wrigley (1935). Nevertheless the studies of Papnicolaou (1928) and Papnicolaou and Traut (1934) on vaginal secretions have popularised it.

LARGE BORE NEEDLE BIOPSY

Needle biopsy to retrieve cells were started by Ward (1914) and Guthric (1929). They aspirated large lymph nodes from a lymphoma patient. Later in 1930s Martin and Ellis reported of diagnosing 6 breast carcinomas from breast lumps. This was also used by Coley, Sharp and Ellis (1931) for bone tumours and by Foster (1931) for central nervous system tumours. The size of the needle used was 18 gauge.Large bore Vilms-Silermann needle was used by Crile and Hawk (1917), Crile, Vickery and Kirstaedter (1920). But this technique was not widely accepted because of limited tissue available for sampling, haemorrhage and fear of implanting the tumour along the needle track.Between 1976 and 1979,a number of studies from North American centers gave impetus for more extensive study of needle biopsy.

Large needle biopsy is restrited to larger lesions more than 2.5 cm,but fine needle aspiration can be used for smaller lesions as small as 0.5 cm. Most thyroid nodules detected on clinical examionation are 1 to 2 m in size for which fine needle biopsy is found to be more faourable.

FINE NEEDLE ASPIRATION CYTOLOGY

Aspiration biopsy cytology is a special branch of diagnostic cytology that interrupts changes in cells extracted from within organs, tumours and non neoplastic abnormal tissues (Joseph and Link 1983).

The technique of fine needle aspiration (FNA) was developed in New York city at Memorial Hospital in the 1920s. Despite the impressive results obtained from this technique it was not accepted in the United States and it was even abandoned in the Memorial Hospital. It was resurrected in the Europe years later, particularly in Scandinavian countries, where its safety and accuracy were fully documented. Eventually it was brought back to United States where later on it was widely used for lesions of thyroid,breast and salivary glands, and lungs. It was carried out with a fine needle and sometimes under image guidance. The procedure was found to be with no doubt inexpensive, safe, quick and when performed in experience hands – quite accurate. It has contributed in a great deal in converting cytology from a mere primary screening tool to a more powerful diagnostic weapon. But like any procedure this technique also has its own limitations.

The terminologies used by various authors were:

Scandinavia : Fine Needle spiration Biopsy (**FNAB**)

North America : Aspiration Biopsy Cytology (**ABC**)

Thompson : Thin Needle Selective Sampling (**TNSS**)

Currently most centers use : Fine Needle Aspiration Cytology (**FNAC**)

ADVANTAGES OF FNAC

1. The technique is safe,simple, painless and acceptable to most patients.
2. It can be done without any preparation or anaesthsia.
3. It takes less than 5 minutes to perform and its interpretation is also rapid with reported within an hour. It thus decreases the need for time consuming and expensive investigations.
4. Representative sample is taken because the needle enters various areas of the nodule, while maintaining negative pressure.
5. If an inadequate sample was obtained in the first instance the technique can be repeated without much patient discomfort.
6. Its an accurate and cost effective investigation and doesnot require hospital admission and can be done in an out-patient basis.
7. Its less traumatic and is of less complications.
8. From this technique definite morphological diagnosis can be made thus annuls the need for diagnostic surgery.

9. Cysts can be aspirated completely and thus it can be therapeutic too in such instances.
10. Underlying thyroiditis can also be detected by this method.

DISADVANTAGES OF FNAC

1. Minimal material is available for examination thus architecture and cell relationship are absent.
2. Due to cystic lesions and cystic areas in thyroid,inadequate material is aspirated in such cases.
3. The needle may miss important areas in the nodule despite a good attempt.
4. Distinction between follicular aadenoma and follicular carcinoma is difficult as it needs capsular and vascular invasion to differentiate between the two. Hurtle cells may also pose the same the puzzle.
5. Good cytopathologist is essential to interpret the results.

Lowhagen et al claims to have studied around 18,000 smears in the past 20 yrs and brought out the following obserations:

1. There is considerable difficulty in differentiating follicular neoplasms from hypercellular nodules, which requires scintigraphy.
2. Difficulty was also experienced in distinguishing between Hashimoto's thyroiditis from malignancy in some aspirates, especially in cases of Hurtle cell metaplasia.

3. In upto 7% of specimens co-existence of malignancy and MNG was noticed on HPE.
4. Inspite of high accuracy of FNAC clinical knowledge should be a guiding factor for the surgeon to decide upon the need for surgery.

ACCURACY OF FNAC (According to the study of Orrel SR et al)

Colloid goiter (simple nodular) – 96%

Hashimoto's thyroiditis – 90 to 95%

Papillary carcinoma of thyroid – 60 to 90%

Follicular carcinoma of thyroid – 70%

Grave's / Plummer's disease – variable (needs clinical and biochemical correlation).

COMPLIATIONS OF FNAC

Eventhough FNAC is considered a simple and safe procedure it may be associated with some complications which are encountered rarely:

1. Local discomfort.
2. Minor hematoma.
3. Injury to carotid artery, internal jugular vein and trachea which is rare.
4. Seeding of tumour along the needle track which is theoretically possible but reported cases in the world literature is anecdotal.
5. Transient nerve palsy.

PITFALLS OF FNAC

Indequatesampling : This could be because of poor cell in aspirate (as in cases of cyst or Hashimoto's thyroiditis or Riedel's thyroiditis) or haemorrhagic(as in adenoma or hyperplastic nodule). So second or a third attempt becomes mandatory. Hamburger and Hamburger pointed out that as the number of samples increased the false negative values decreased. They therefore recommend a minimum of six aspirates before declaring the slide inadequate. The percentage of unsatisfactory smears from various studies is found to be 0 to 20 %.

1. Geographical misses : This can occur. In such instances prior ultrasound or scindiscan can delineate the area of interest for study. A finerappot between the clinician and the pathologist can reduce such errors.
2. Interpretational inaccuracies : Interpretation depends on the experience of the cytopathologist.

Aschroft and Van Harley had certain criterias for centers doing FNAC :

- Adequate proficiency is defined as providing each operator with 100 to 200 smears for the familiarity of the procedure.
- One should examine not less than 10 smears per week or 500 smears per year.

If the input is decreased, the number of false positives and false negatives increases because of lack of experience.

False negative interpretations are of real concern as they are important in cases of malignancies.

CORE NEEDLE BIOPSY

Biopsy with large bore needles like VilmsSilvermann and Trucut needle are used by some to increase the accuracy. Use of large needles preserves the architecture and cytology of the lesions, which are important before declaring a smear inaccurate. But the procedure is limited to larger lesions and it requires more skill and is associated with more complications. Core needle biopsy doesnot solve the issue of atypical cells or the question of capsular and vascular invasion of follicular neoplasm.

PATHOLOGY

A normal thyroid gland is not palpable. The term goiter (*latin gutter= throat*) is used to describe generalised enlargement of thyroid gland. A discrete swelling (nodule) in no other palpable abnormality in the thyroid gland is termed as solitary or isolated swelling.Discrete swelling with abnormality elsewhere in the gland is termed as dominant. Thyroid enlargement can be categorized as follows :

CLASSIFICATION OF THYROID SWELLINGS

1. Simple goiter (Euthyroid)
    - ✓ Diffuse hyperplastic
        - Pubertal
        - Physiological
        - Pregnancy
    - ✓ Multinodular goiter
2. Toxic
    - ✓ Toxic adenoma
    - ✓ Multinodular
    - ✓ Diffuse- Graves disease
3. Neoplastic
    - ✓ Benign
        - Follicular adenoma
        - Papillary adenoma
        - Atypical adenoma
        - Hyalinisingtrabeculated adenoma
    - ✓ Malignant
        - Papillary carcinoma
        - Follicular carcinoma
        - Medullary carcinoma

- Anaplastic carcinoma
- Poorly differentiated carcinoma

4. Inflammatory

✓ Autoimmune

- Chronic lymphocytic thyroiditis
- Hashimoto's thyroiditis

✓ Granulomatous

- De Quervain's thyroiditis

✓ Fibrosing

- Reidel's thyroiditis

✓ Infective

- Acute – Bacterial thyroiditis

  Viral thyroiditis

  Subacute thyroiditis

- Chronic – Tubercular, Syphilitic, etc.

✓ Others

- Amyloid

DIAGNOSIS

The diagnosis of thyroid diseases is based on the evaluation of thyroid functions, hyperthyroid or hypothyroid and based on the nature of the lesion, benign or malignant.

INVESTIGATIONS *ESSENTIAL*

A) Serum

TSH (T_4 and T_3, if abnormal)

TAA (Thyroid auto antibodies)

B) FNAC

Fine needle aspiration cytology of all discrete palpable swellings.

OPTIONAL

A) Calcium and albumin

B) Chest radiography and thoracic inlet if there is tracheal deviation or retrosternal extension

C) Ultrasound of neck (CT and MRI are rarely indicated)

D) Isotope scan if discrete swelling and toxicity co-exist.

TESTS OF THYROID FUNCTION

A multitude of tests are available to evaluate thyroid functions but no single test is sufficient to assess the thyroid functions in all situations.

Serum TSH

Serum TSH levels (0.5 to 5 microU/ml-normal) can be measured to even very low concentrations by radiochemiluminometric assay.

The ultrasensitive assays can detect TSH levels as low as 0.01 microU/ml. serum TSH levels reflect the ability of the anterior pituitary to detect the levels of free T_4 levels. There is an inverse relationship of free T_4 level and logarithm of TSH concentration.Even small changes of free T_4 lead to large shift in TSH levels. So, the ultrasensitive TSH levels have become more sensitive and specific test for the diagnosis of hypo or hyperthyroidism,and for optimizing the T_4 suppressive and replacement therapy.

Triiodothyronine(T_3) and Thyroxine (T_4)

The total T_4 (referencerange- 55 to 150 nmol/L) and T_3 (reference range -1.5 to 3.5 nmol/L) leels are measured by radioimmunoassay. It measures both the free levels and bound levels of the hormones. Only a small levels of both T_3 and T_4(0.03% of T_4 and 0.3% of T_3) are free and physiologically active. Highly accurate radioimmunoassay of free T_3 and T_4 are now routinely done. T_3 toxicity (with a normal T4) is a separate entity and is diagnosed by measuring the serum T_3, although a suppressed TSH with a normal T_4 level is suggestive.

THYROID ANTIBODIES

These include anti-thyroglobulin (anti-Tg), antimicrosomal or antithyroid peroxidase (anti- TPO) and thyroid stimulating immunoglobulins (TSI). They are used to determine the cause of thyroid dysfunction and swellings. Auto immune thyroiditis is associated with euthyroid goiter or failure or thyrotoxicity. Levels above 25 units per ml of TPO antibody and titres above 1:100 for antithyroglobulin are considered significant, but a propotion of patients with histological evidence of lymphocytic (auto-immune) thyroiditis may be seronegative.

SERUM THYROGLOBULIN

Thyroglobulin is normally not released into circulation in large amounts, but its levels increases dramatically in destructive processes of thyroid like thyroiditis or in overactive states like Graves disease and toxic multinodulargoitre. The most important use of thyroglobulin is in monitoring the patients with differentiated thyroid cancer following total thyroidectomy or radioactive iodine ablation for recurrence.

ISOTOPE SCANNING

Both iodine -123(^{123}I) and iodine 131 (^{131}I) are used to image thyroid.^{123}I emits low dose iodine which can be used to image lingual thyroid or goitre. ^{131} I produces higher dose of radiation exposure and its used to treat patients with differentiated thyroid cancer for metastatic disease.

Routine use of isotope scan is not routinely necessary and is inappropriate for distinguishing benign from malignant lesions because majority (80%) of cold swellings are benign and some (5%) functioning or warm swellings are malignant. Its main use is in the toxic patient with a nodule or nodularity of thyroid. Localization of overactivity in the gland will differentiate a toxic nodule and also in a toxic MNG with several areas of increased activity in the gland.

Technetium – 99m (^{99m}Tc) pertechnetate is also used for thyroid evaluation and it has a shorter half- life and minimum radiation exposure. Its particularly sensitive to nodal metastasis.

ULTRASOUND

Its an excellent noninvasive imaging modality. It is helpful in thyroid nodules to distinguish between sloid and cystic lesions. It also provides information about size and multicentricity. It is also used to assess cervical lymphadenopthy and to guide fine needle aspiration (FNA) biopsy ,especially B-mode that can be used preoperatively and intraopertively.

CT / MRI SCAN

It gives excellent view of the thyroid gland and the adjacent lymph nodes. It is particularly useful in evaluating large, fixed and substernal goiters and their relationship with trachea nd vascular structures. Non-contrast CT should be done in patients with possibility of further radioactive iodine therapy.

FNAC and HPE of THYROID LESIONS

1. Low cellular smears are benign and high cellular smears are suspicious.
2. Degerative changes and old haemorrhages are seen as histiocytes, which are seen as large cells with peripherally pushed pyknotic nuclei and cloudy cytoplasm, with many vacuoles and granules of degraded or digested material.
3. Hurtle cells look longer than follicular cells, with well defined cellular borders, granular cytoplasm and moderate to large nulei.
4. Inflammations.

A. Suppurative thyroiditis

Acute suppurative thyroiditis from bacterial infections is rare. The aspirates are highly cellular consisting of neutrophils,macrophages and cellular debris.

B. Sub acute (de Quervain's thyroiditis)

Aspirates demonstrate presence of lymphocytes, plasma cells,epitheloidhistiocytes and multi nucleated giant cells containing 30 – 300 nuclei.

C. Hashimoto's thyroiditis

Lymphocytic thyroiditis (Hashimoto's thyroiditis) is an auto immune disease that can present as diffuse enlargement of thyroid or as solitary or multiple nodules. Fine needle aspiration usually consist of numerous

lymphocytes and plasma cells with follicular cells showing oncocytic features (Hurtle cells). Hurtle cells contain dense abundant granular cytoplasm and may possess hyperchromatic highly atypical nuclei. The recognition of Hashimoto's thyroiditis is difficult for the cytopathologist, especially when only inflammatory or and epithelial components are present. This can produce false positive diagnosis of lymphoma or carcinoma, especially Hurtle cell tumour.

D. Riedel's struma

The aspirate contains mature lymphocytes and some fibroblasts.

BENIGN NON NEOPLASTIC LESIONS

A. Non toxicGoitres

1) SIMPLE GOITRE (COLLOID GOITRE)

The smear is scanty or moderately cellular with large amounts of colloid and epithelial cells, the cells are arranged in discrete fashion, in clusters and in sheets.

2) MULTINODULAR GOITRE

Smear shows plenty of colloid in the background of which, epithelial cells are found in microfollicle formation and cyst macrophages together gives a chess board pattern. Hemosiderin laden macrophages and histiocytes are usually conspicuous. Microscopically, there is partially or completely encapsulated nodules ,which exhibit focal cystic degeneration and necrosis.

There is colloid distended follicles of various sizes and shapes separated by fibrous bands.

B. Toxic goitre

Smears are bloody with flare cells,naked nuclei and follicular cells with abundant finely granular cytoplasm and peripheral vacoules.

Follicles are of diversified size and shape with variable amounts of colloid.

Epithelium is highly columnar,sometimes multilayered, and may protrude into the lumen,suggesting a papillary neoplasm.

NEOPLASMS

A. Follicular neoplasm

Cytologicallyits quite difficult to differentiate between follicular adenoma and follicular carcinoma. Unless vascular and capsular invasion is evident it is difficult even in histology. Hence both follicular adenoma and carcinoma are both excised. The following are certain distinguishing features:

a) Follicular adenoma

The aspirate contains scanty colloid. The cells have microfollicular structure with small, round,and uniform nuclei.

b) Follicular carcinoma

The aspirate is bloody with isolated follicules or follicles which are laid in small sheets. The cellsshowsatypia to frankly malignant transformation. The nuclei are large, oval and eccentric,better appreciated by

plantimeteric study. Benign lesions demonstrate honey-comb,two dimensional sheets of follicular cells, three dimensional over lapped, crowded cells indicate well differentiated follicular carcinoma.

Histologically, it may be apparently encapsulated or diffusely infiltrating, well or poorly differentiated. It is differentiated morphologically from adenoma by capsular and vascular invasion.

Papillary carcinoma

Papillary carcinomas may present as solitary or multifocal lesions within the thyroid. They may be well circumscribed and even encapsulated; sometimes it infiltrate the adjacent parenchyma with ill-defined margins. On the cut surface, they may appear granular and may sometimes contain grossly discernible papillary foci.

The diagnosis of papillary carcinoma is based on nuclear features even in the absence of a papillary architecture. The nuclei of papillary carcinoma cells contain very finely dispersed chromatin, which imparts an optically clear appearance, giving rise to the so called "ground-glass" or "Orphan Annie eye" nuclei. The invaginations of the cytoplasm may give the appearance of intranuclear inclusions (hence the term pseudo-inclusions) in cross-sections. Concentrically calcified structures termed ‘psammoma bodies’ are present within the papillae.

B. Medullary carcinoma

Microscopically, smears of medullary carcinomas are composed of polygonal to spindle-shaped cells. They may form nests, trabeculae, and even follicles. Acellularamyloid deposits**,** derived from altered calcitonin molecules, are present in the adjacent stroma in most cases and are a distinctive feature of these tumors. Calcitonin is readily demonstrable both within the cytoplasm of the tumor cells and in the stromal amyloid by immunohistochemical methods. Electron microscopy reveals variable numbers of intracytoplasmic membrane-bound electron-dense granules. One of the peculiar features of familial medullary carcinomas is the presence of multicentric C-cell hyperplasia in the surrounding thyroid parenchyma, a feature which is usually absent in sporadic lesions.

C. Anaplastic carcinoma

Microscopically, anaplastic neoplasms are composed of highly anaplastic cells, which may take on several histologic patterns, including

(1) Large, pleomorphic giant cells;

(2) Spindle cells with a sarcomatous appearance;

(3) Mixedspindle and giant-cell lesions; and

(4) Small cells**,** resembling those seen in small-cell carcinomas at other sites.

Most of the "anaplastic small-cell" tumors are ultimately proved to be medullary carcinomas or malignant lymphomas.

Foci of papillary or follicular differentiation may be present in some, suggesting origin from a better differentiated carcinoma.

D. Hurtle cell neoplasms

Hurtle cell adenoma

It is a variant of follicular neoplasm, smear demonstrates large follicular cell devoid of follicular structures. Microscopically it contains follicules with regular epithelium,colloid may be abundant or absent.

Accurate distinction between benign and malignant Hurtle cell tumours is difficult. The cells are oval to polyhedral with abundant granular cytoplasm and a prominent large eccentric nucleus.

The cells are isolated or arranged in loose groups, marked nuclear pleomorphism indicates malignancy.

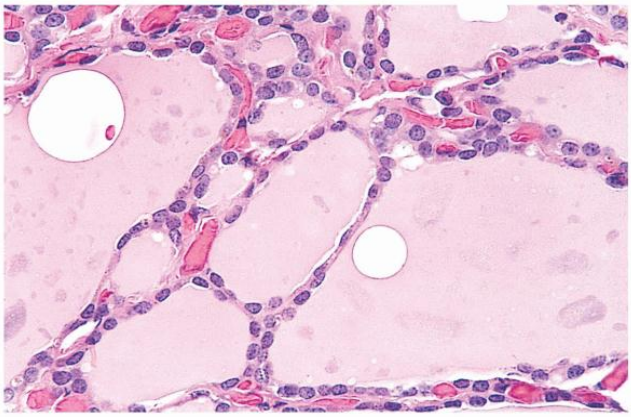


Fig. 10.**Normal thyroid follicle lined by thin layer of cuboidal follicular epithelial cells**

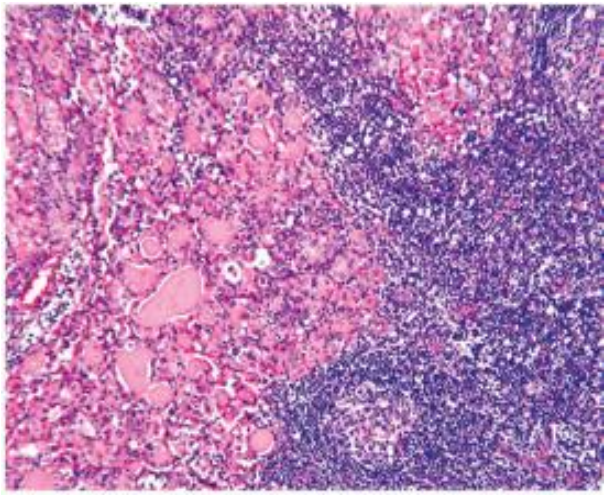


Fig. 11.**Hashimotos thyroiditis**

Fig. 12 .**Gross specimen of follicular adenoma**.

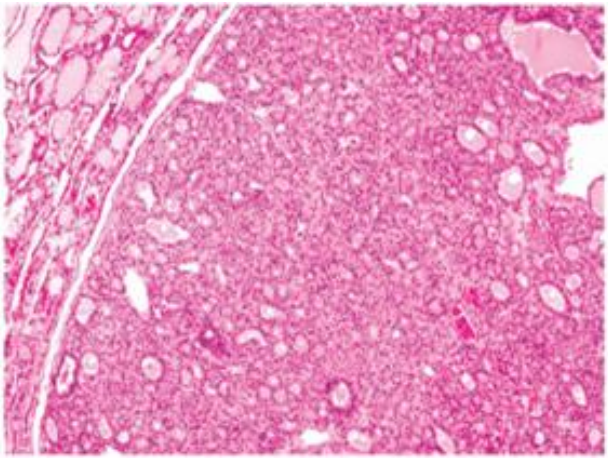


Fig. 13.**Follicular adenoma with no capsular or vascular invasion.**

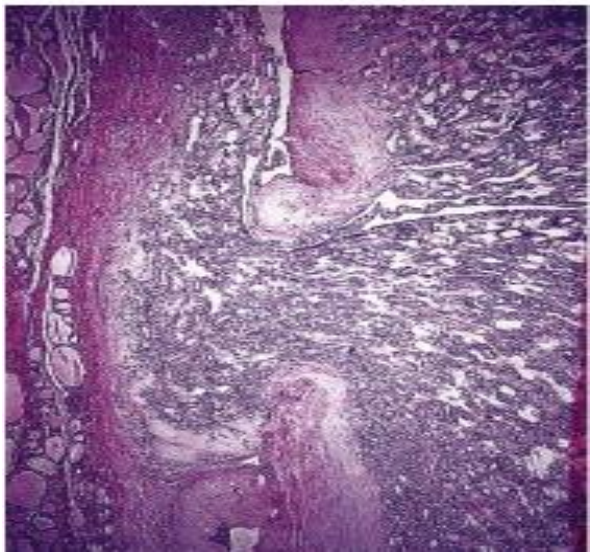


Fig. 14.**Capsular invasion of follicular carcinoma**.

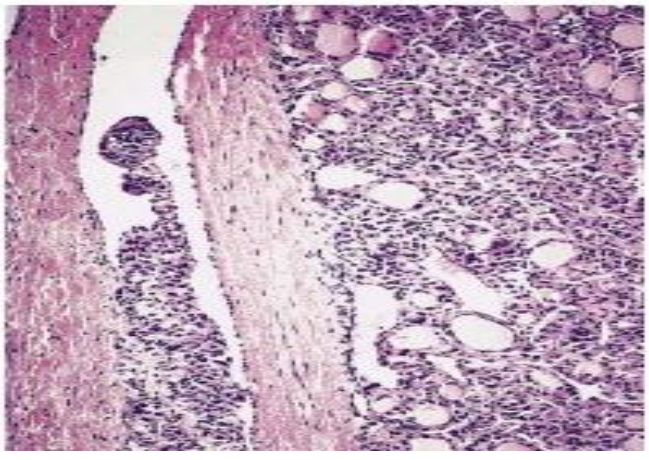


Fig. 15 **Vascular invasion of follicular carcinoma**.

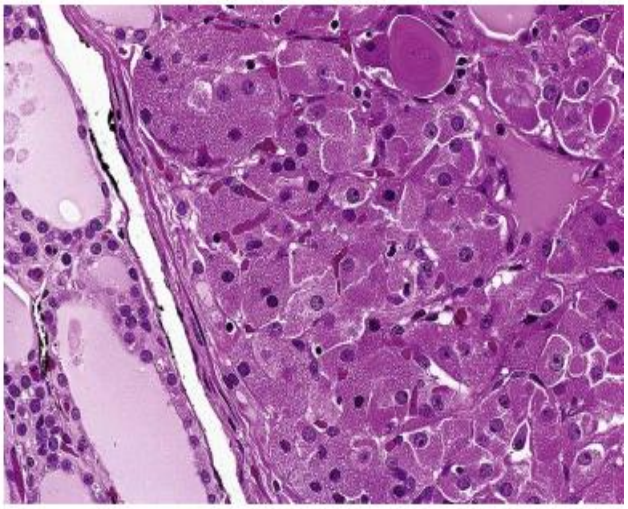


Fig. 16 **Hurtle cell adenoma**

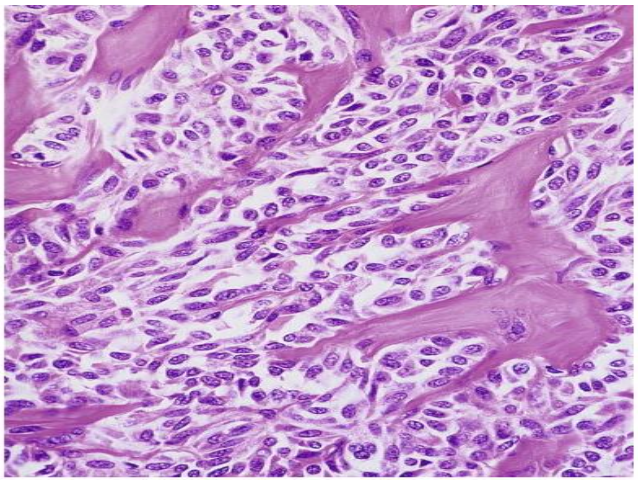


Fig.17 **Medullary carcinoma with amyloid stroma.**

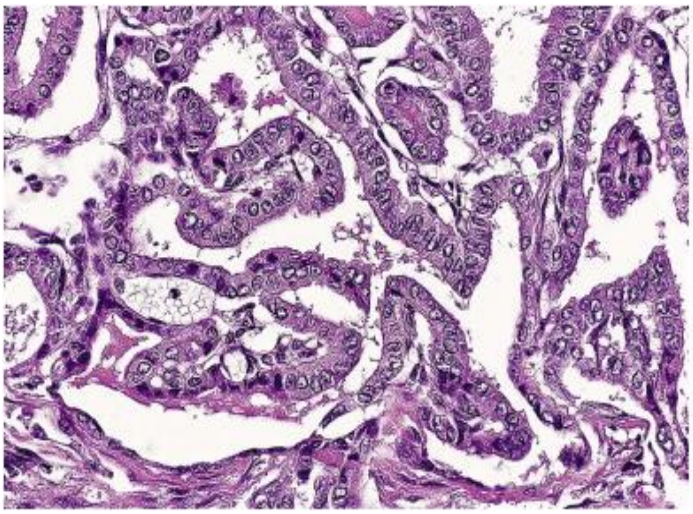


Fig. 18 **Papillary carcinoma**

METHODOLOGY

The study includes those patients admitted in the surgical wards of Tirunelveli Medical College Hospital from January 2012 to June 2013 for treatment of thyroid diseases.

Study design **:** A prospective study.

Place **:** Tirunelveli Medical College Hospital

Study period **:** From January 2012 to June 2013.

Source of data **:** Patients with thyroid swelling having clinical and sonological indication for FNAC and subsequent thyroid surgery admitted in the wards of Department of Surgery,Tirunelveli Medical College Hospital during the study period.

Sample size and method:

A total of 100 patients with thyroid swelling were studied.

SELECTION CRITERIA

INCLUSION CRITERIAS

The study includes those patients-

1. Getting admitted in the surgical wards for the treatment of various thyroid diseases.
2. The Thyroid Function Tests(TFT) normal.
3. Who are willing to co-operate for the study.

EXCLUSION CRITERIAS

The study excludes those patients with-

1. Bleeding disorders.
2. Reduced TSH levels.
3. Pregnant ladies and children below 12 years.
4. Not willing for surgery.
5. Lost for follow up.

Patients with goitrewas evaluated clinically. Relevant aspects of patient's history included age, sex, rapidity of growth, recent onset of hoarseness, dysphagia, dyspnoea, symptoms of hypo or hyperthyrodism, history of head and neck irradiation, family history of endocrine diseases was included.

Physical examination to determine whether the gland was diffusely enlarged, solitary, nodular or multinodular with symmetric or asymmetric

enlargement was done. In nodular swelling, the size, shape, consistency, location and mobility was assessed. The patient was also be examined for the presence of cervical lymphadenopathy.

A thyroid function test and an ultrasound was performed using a 7.5 MHZ high frequency linear array transducer. An informed consent after explaining the procedure and its complications namely pain and haemorrhage was obtained.

The procedure was carried out in the Department of Pathology Tirunelveli Medical College Hospital.

MATERIALS USED

1. SYRINGE : 10ml disposable plastic syringe
2. NEEDLE : 23G disposable needle
3. MICROSLIDES : 7.5 x 2.5 cm in size
4. FIXATIVE : 95% isopropyl alcohol
5. SPIRIT SWAB : To sterilize the skin
6. STAIN : Hematoxylin and eosin

PROCEDURE

The patient was placed supine with neck extended and instructed not to swallow or talk. The skin cleansed with a simple alcohol preparation. Proper site for aspiration decided, avoiding, superficial neck vein. Under visual

guidance a 23 gauge needle was introduced into the nodule with a series of rapid advance - withdraw motions. Patients were subjected to 2-5 passes when sample are adequate or 5-8 passes when assessed inadequate initially. In patients with lymphnodes FNAC was taken from lymphonodes also and later correlated with lymphnode biopsy. Pressure is applied over the biopsy site to minimise bruising and decrease the chance of haematoma. The sample is expelled on to a clean, dry, microscopy slide using air in a syringe taking care to avoid splashing. Smears are quickly dried and placed in Coplin jars with isopropyl alcohol.Alcohol fixed smears was then treated with Haematoxylin and Eosin and examined under the microscope.

Results of fine needle aspiration cytology can be classified as :

1. Malignant
2. Indeterminate or suspicious
3. Benign
4. Nondiagnostic.

RESULTS

The **results** of the **100 patients** studied with their **FNAC and HPE** is as follows:

Age and Sex distribution

Table : 1

Age and Sex distribution

AGE(yrs)	MALE	FEMALE	TOTAL	%
10 TO 20	2	5	7	7
21 TO 30	3	21	24	24
31 TO 40	1	31	32	32
41 TO 50	1	14	15	15
51 TO 60	3	13	16	16
61 TO 70	2	3	5	5
71 TO 80	0	1	1	1
TOTAL	**12**	**88**	**100**	**100**

Fig. 19. SEX DISTRIBUTION

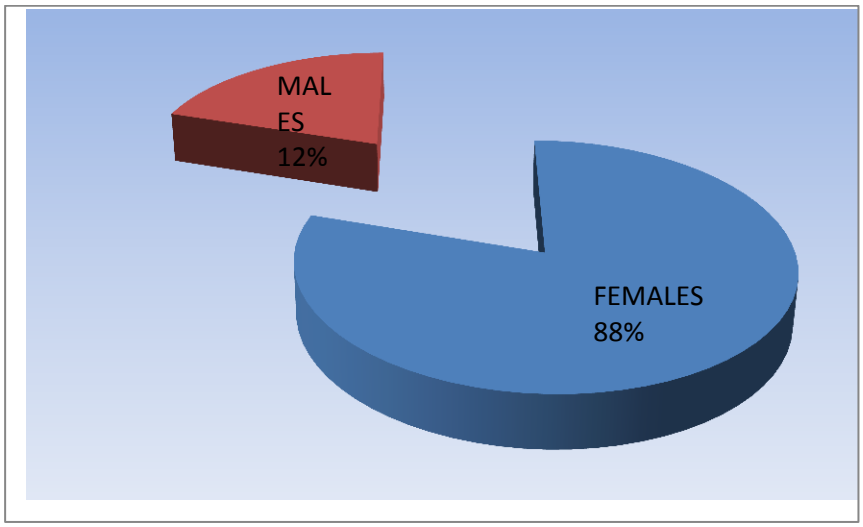
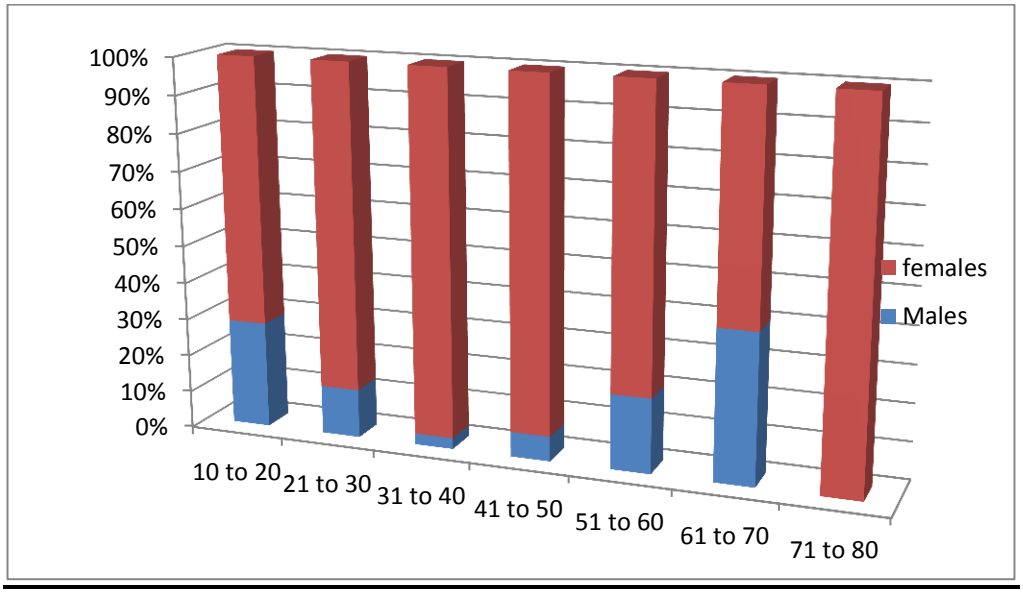


Fig. 20. AGE DISTRIBUTION



SEX INCIDENCE

The study consisted of a total of 100 patients among whom, 88 were females and 12 were males.

FEMALES : 88

MALES : 12

Females : Males = 7.3 : 1

AGE DISTRIBUTION

The study group of 100 patients included cases ranging from 12 yrs to 75 yrs.

Majority of thyroid cases (56%) were in the 2nd and 3rd and decades of life (21-40) yrs.

CYTOLOGICAL DIAGNOSIS

Of the 100 cases of thyroid selected for study, 86 were cytologically benign and 14 were malignant.

Among the benign thyroid swellings 37 weremultinodulargoitres, 22 colloid goitres, 21 Hashimotos thyroiditis, 5 follicular neoplasm and one was Hurtle cell neoplasm.

Of the 14 malignant thyroid lesions, 13 were papillary carcinoma and one was small cell variant of medullary carcinoma.

Of the 100 excised specimens, 82 were confirmed to be benign and 18 were malignant.

Among the benign ones,25 were multinodulargoitres, 24 were thyroiditis, 13 were follicular adenoma, 10 were colloid goitre, 9 were microfollicular adenoma, and one was Hurtle cell adenoma.

Among the malignancies, 15 were papillary carcinoma thyroid, one follicular carcinoma, one anaplastic carcinoma, and one turned out to be small cell variant of medullary carcinoma.

Of the 18 malignancies diagnosed histologically as malignant, 14 were diagnosed correctly from cytology too. But four were found to be benign in cytological study.

Of the 12 male patients studied, 8 had benign lesions, and 4 had malignant lesions.

Among the benign ones, 4 had multinodulargoitre,3 Hashimotos thyroiditis, one colloid goitre, and of the malignancies, 3 were papillary carcinomas and one turned out to be anaplastic carcinoma.

The accuracy of FNAC in the diagnosis of malignant disease of thyroid was evaluated by using the predictive value theory. Thesensitivity,specificity,positive and negative predictive values and accuracy were determined.

Predictive Value of FNAC of Thyroid Swellings

Table – 2

2×2 TABLE FOR THE STUDY

Cytology	Histology		Total cytology
	Benign	Malignant	
Benign(no malignant cells)	82	4	86
Malignant (malignant cells)	0	14	14
Total histology	**82**	**18**	**100**

True negative (TN) - 82

True positive (TP) - 14

False negative (FN) - 4

False positive (FP) - 0

Sensitivity : Positive in disease $= \frac{TP \times 100}{TP + FN}$

$= \frac{14 \times 100}{18}$

= **77.78%**

Specificity : Negative in disease $= \frac{TN \times 100}{TN + FP}$

$= \frac{82 \times 100}{82}$

= **100%**

Positive predictive value $= \frac{TP \times 100}{TP + FP}$

$= \frac{14 \times 100}{14}$

$=$ **100 %**

Negative predictive value $= \frac{TN \times 100}{TN + FN}$

$= \frac{82 \times 100}{86}$

$=$ **95.35 %**

ACCURACY $= \frac{TP + TN \times 100}{TP + TN + FP + FN}$

$= \frac{96 \times 100}{100}$

$=$ **96%**

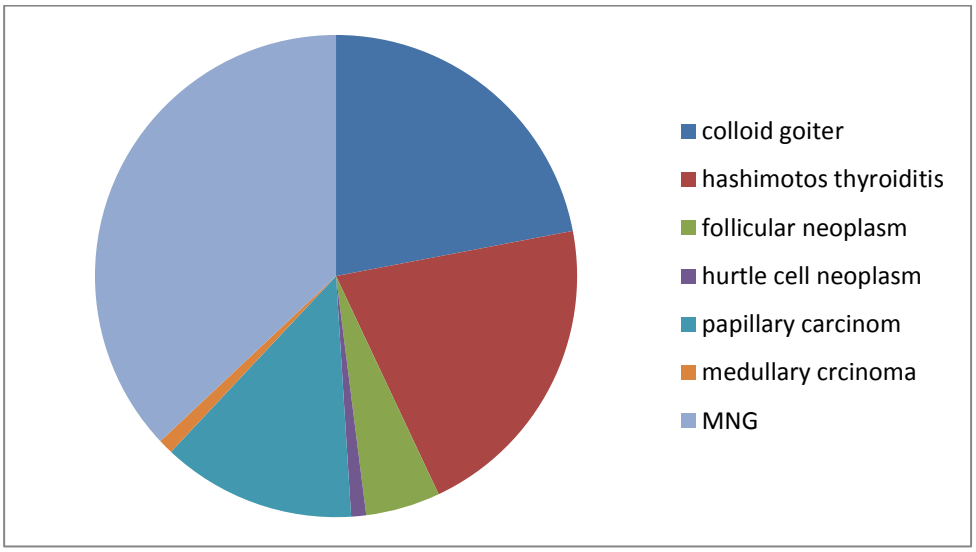
FINE NEEDLE ASPIRATION CYTOLOGY DIAGNOSIS

Table -3

FINE NEEDLE ASPIRATION CYTOLOGY DIAGNOSIS

FNAC Diagnosis	Number	Percentage
MULTINODULAR GOITRE	37	37
COLLOID GOITRE	22	22
HASHIMOTOS THYROIDITIS	21	21
FOLLICULR NEOPLASM	5	5
HURTLE CELL NEOPLASM	1	1
PAPILLARY CARCINOMA	13	13
MEDULLARY CARCINOMA	1	1

Fig.21. FNAC DIAGNOSIS



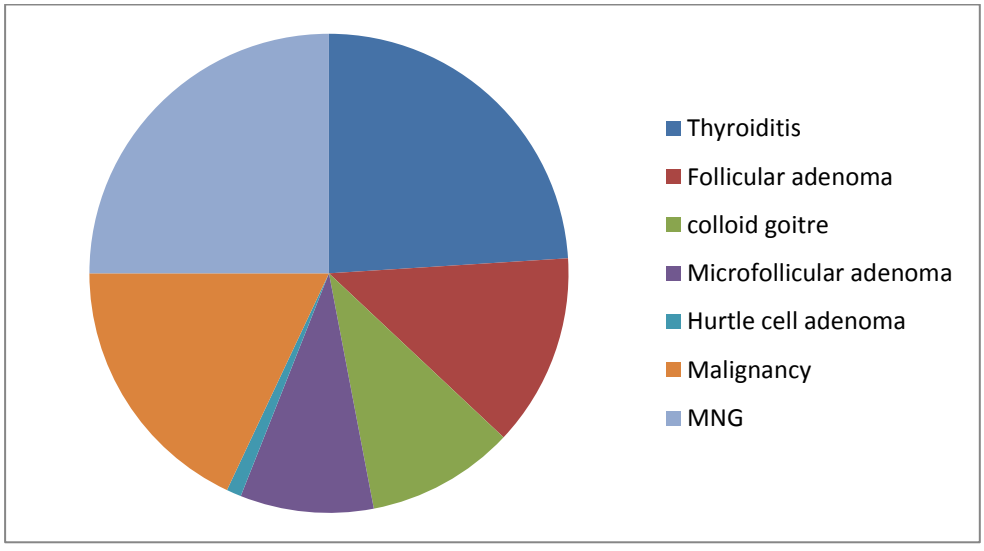
HISTOPATHOLOGICAL DIAGNOSIS

Table – 4

Histopathological Diagnosis

HISTOPATHOLOGICAL DIAGNOSIS	NUMBER	PERCENTAGE
MULTINODULAR GOITRE	25	25
THYROIDITIS	24	24
FOLLICULAR ADENOMA	13	13
COLLOID GOITRE	10	10
MICROFOLLICULAR ADENOMA	9	9
HURTLE CELL ADENOMA	1	1
MALIGNANCY	18	18

Fig. 22. HISTOPATHOLOGICAL DIAGNOSIS



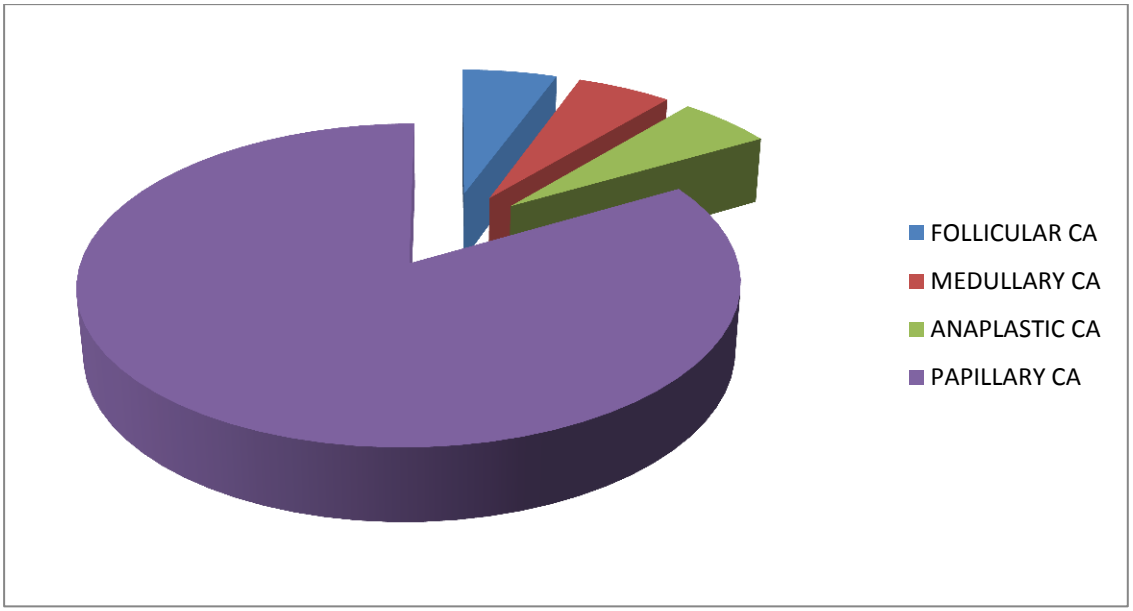
MALIGNANCY IN HISTOPATHOLOGY

Table – 5

Malignancy in Histopathology

MALIGNANCY	NUMBER	PERCENTAGE
PAPILLARY CARCINOMA	15	78.94
FOLLICULAR CARCINOMA	1	5.26
MEDULLARY CARCINOMA	1	5.26
ANAPLASTIC CARCINOMA	1	5.26
TOTAL	**18**	**100**

Fig . 23. MALIGNANCY IN HISTOPATHOLOGY



DISCUSSION

AGE DISTRIBUTION

The age of the patients in the present study varied from 12 to 75 yrs.Colacchio et al (1980) studied patients from 30 to 60 yrs. The age of the patients studied by Klemi PJ et al (1990) studied ranged from 21 to 86 yrs. In this study patients of 2^{nd} and 3^{rd} decade was found to be 56%. In the same age group Pandid AA and Kinare (1986) have reported 62%. For the age group of 20 to 60 yrs Starvic GD et al (1980) and Colacchio showed 72% and 60% respectively. The majority of patients in the study conducted by Tabaqchali et al (2000) and Scalbas GM et al (2003) were between 30 and 50 yrs. The study conducted by Rajpurohit (2010) included patients between 16 and 80 yrs.

SEX RATIO

The sex ratio in the present series was 7.3 : 1 with 88 women and 12 men.In the series of Gershengom et al (1977) female to male ratio was 28:5,Harsoulis et al (1986) series was 9:1, and the male proportion in Colacchio series was 16% . In Pandid and Kinare (1986) series female to male ratio ws 58:26, Klemi et al (1990) was F :M is 8:1, and in the study of Rajpurohit (2010) series F:M was 7.66:1. High frequency of women was seen in the present series.

INCIDENCE OF MALIGNANCY

18 out of 100 patients (18%) studied were malignant. The other series shows Chu et al (1979) 26%, Lowhagen et al (1979) 20%, Colacchio et al (1980) was 16%, Silver et al (1981) 22%, Braun and Silver (1984) 18%, Harsoulis et al (1986) 19%, Klemi et al (1990) 11.8%, Godinho L et al (1992) 21%, Pommata et al (19970 35.55%, and Sclabas G M et al (2003) 32% and Rajpurohit series showed 10%.

Among the malignant lesions, papillary carcinoma comprised 79%, follicular,medullary and anaplastic comprised 5% each. Papillary carcinoma was frequent in the 3rd and 4th decades, while follicular carcinoma was seen in the 4th decade and medullary and anaplastic carcinoma was frequent in the 5th and 6th decades. The frequency of carcinomas studied in the series of Stavic et al (1980) and Braun and Silver (1984) 38:25% and 37:29% respectively for papillary and follicular carcinomas respectively. The incidence of papillary carcinomas ws high in the strudy Ramaciottio et al (1984) was 76% and also Harsoulis (1986) was 70% and Klemi et al was 59%. In the study of Sclabas GM (2003) papillary carcinoma was 82% and follicular carcinoma accounted to be 15 %, and the study of Rajpurohit showed papillary and follicular was 77 and 7.7% respectively, which is almost similar to the present series.

AGE DISTRIBUTION OF THYROIDSWELLINGS IN PRESENT SERIES

Table - 6

AGE (yrs)	MNG	THYROIDITIS	FOLLICULAR ADENOMA	COLLOID GOITRE	MICROFOLLICULAR ADENOMA	HURTLE CELL ADENOMA	PAPILLARY CA	MEDULLARY CA	FOLLICULAR CA	ANAPLASTIC CA	TOTAL (%)
10 - 20		2	1	3	1						7
21- 30	5	5	4	2	4	1	3				24
31 -40	10	8	6	2	1		5				32
41 - 50	3	6	1	3	1				1		15
51 - 60	4	3	1		1		5	1		1	16
61 -70	3				1		1				5
71 - 80							1				1
TOTAL (%)	**25**	**24**	**13**	**10**	**9**	**1**	**15**	**1**	**1**	**1**	**100**

Fig. 24 AGE DISTRIBUTION OF NON-NEOPLASTIC LESIONS IN PRESENT SERIES

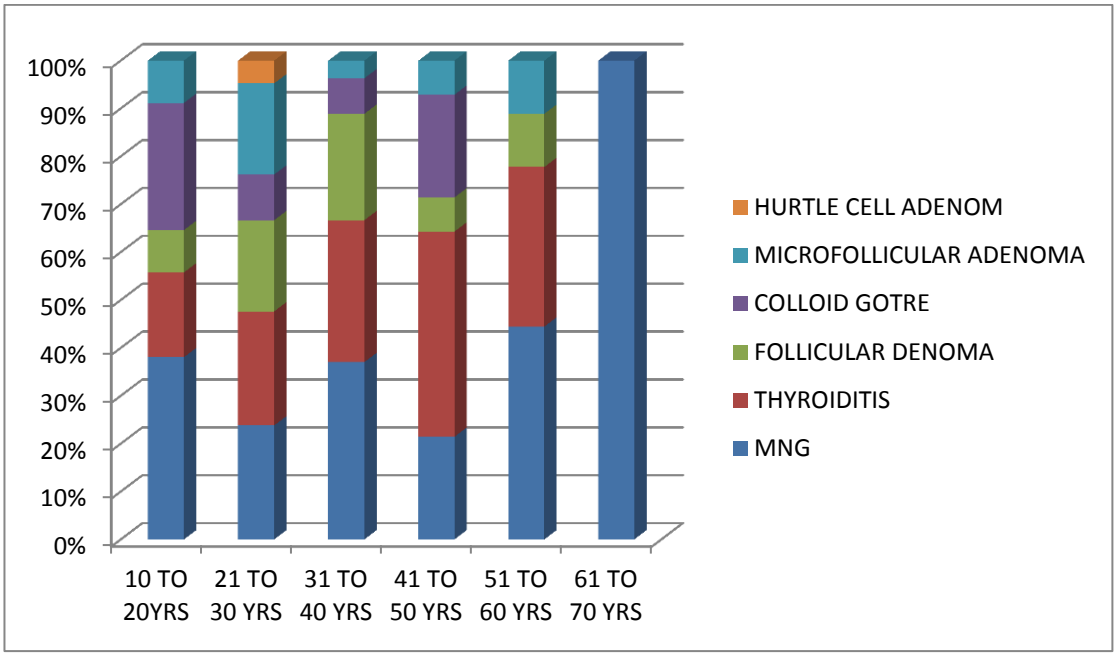
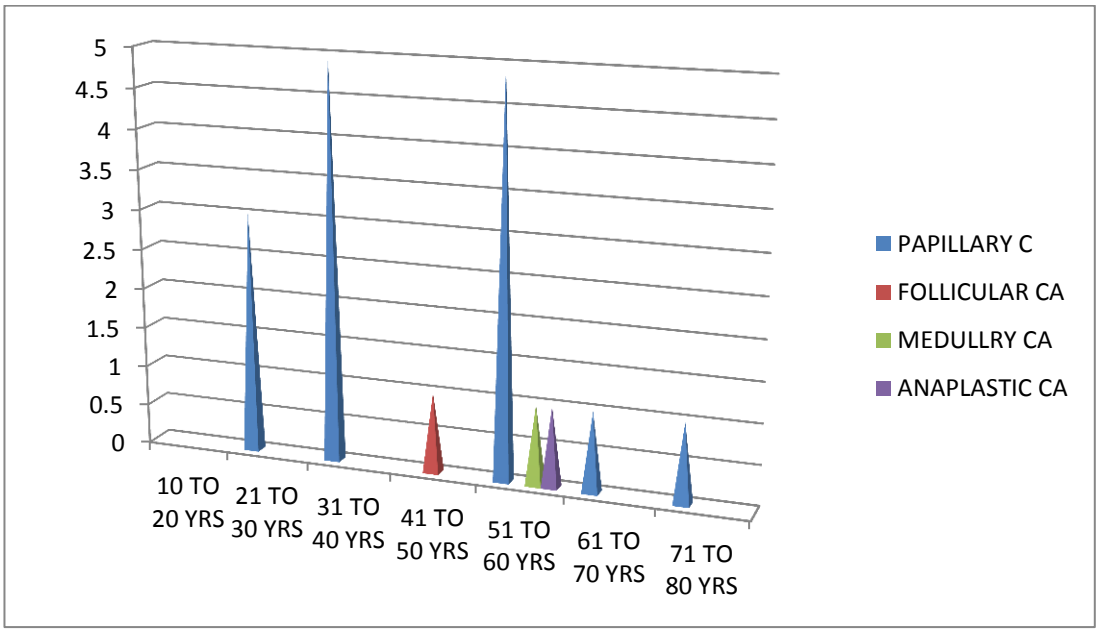


Fig. 25 AGE DISTRIBUTION OF NEOPLASTIC LESIONS IN THE PRESENT SERIES



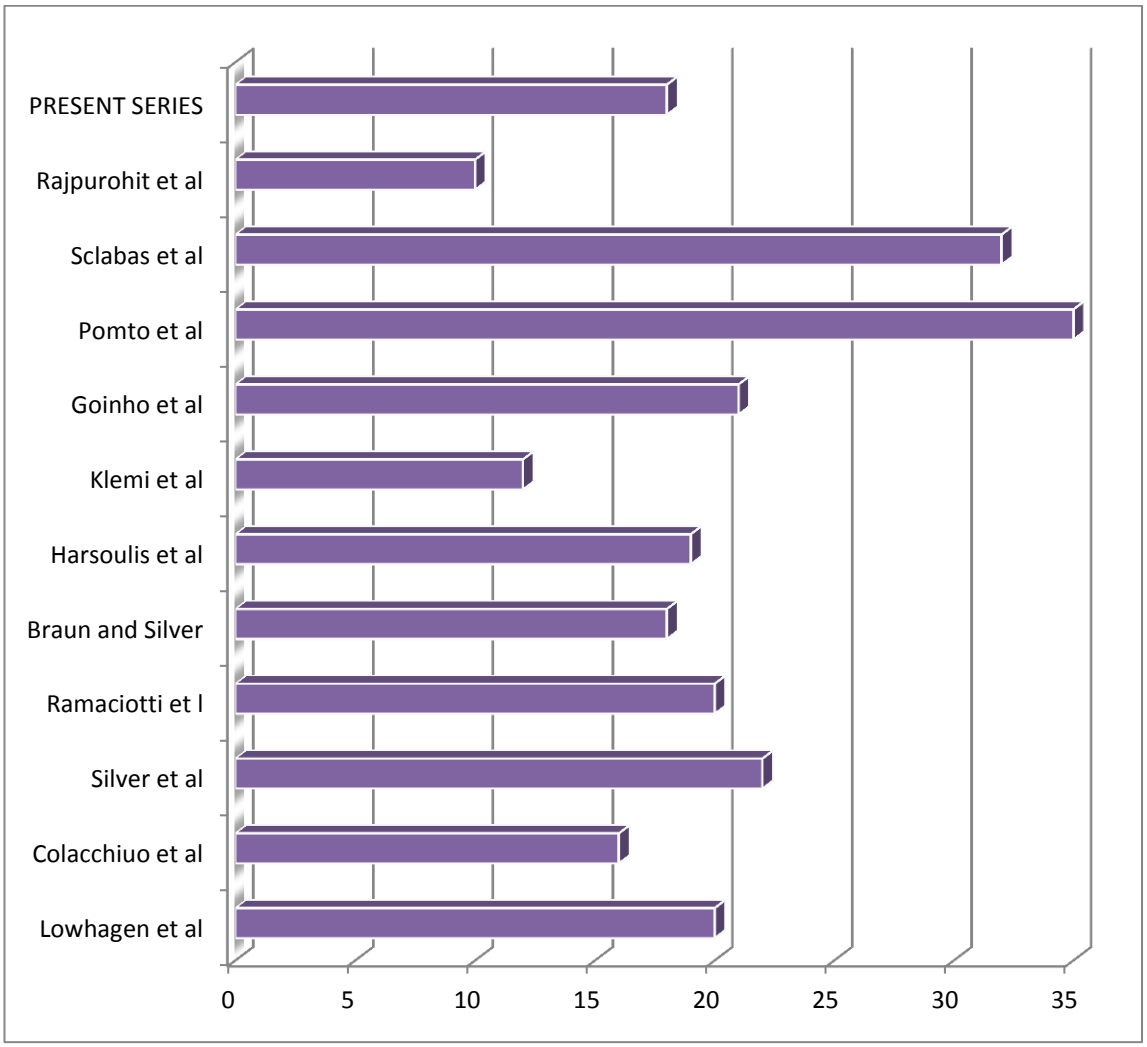
FINE NEEDLE ASPIRATION CYTOLOGY OF THYROID

SWELLINGS : Incidence of malignancy in different series

Table - 7

Sl.No.	Name of the Author	Year	Incidence of malignancy
1	Chu et al	1979	26%
2	Lowhagen et al	1979	20%
3	Colacchio et al	1980	16%
4	Silver et al	1981	22%
5	Ramaciotti et al	1984	20%
6	Braun and Silver	1984	18%
7	Harsoulis et al	1986	19%
8	Klemi PJ et al	1990	12%
9	Godinho et al	1992	21%
10	Pomato et al	1997	35%
11	Sclabas et al	2003	32%
12	Rajpurohit et al	2010	10%
13	PRESENT SERIES	2013	18%

Fig . 26. FNAC OF THYROID LESIONS : Incidence of malignancy from different series

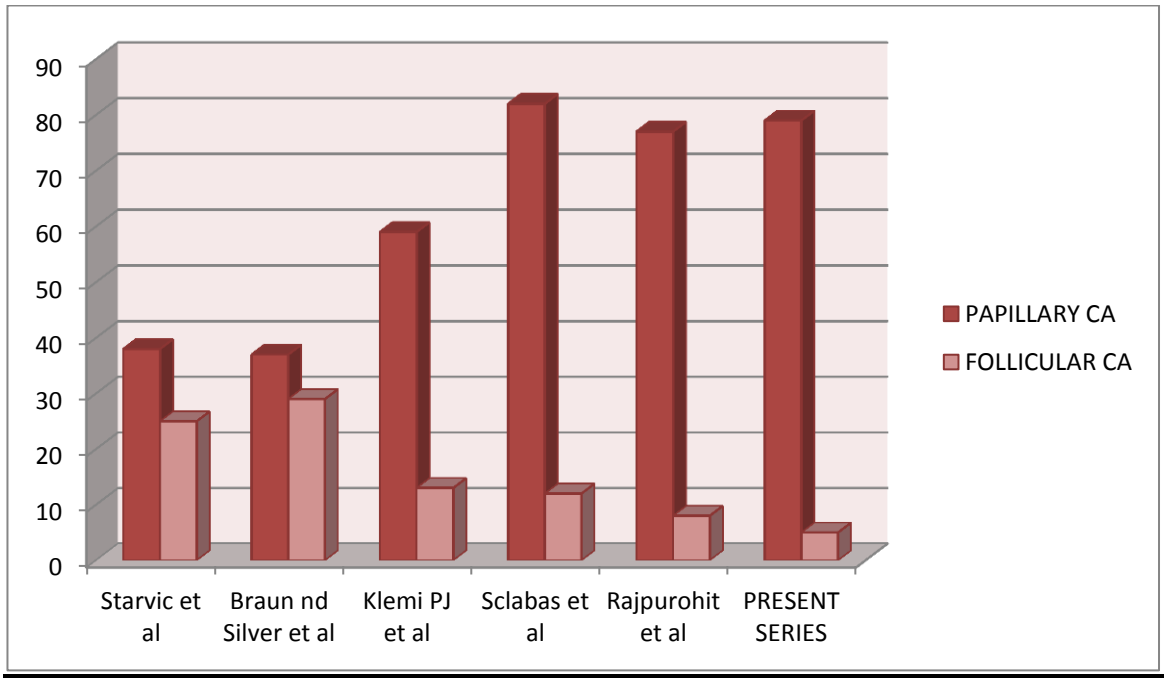


Incidence of malignant histological types from different series

Table - 8

Sl.No.	Name of the Author	Year	Papillary Carcinoma	Follicular Carcinoma
1	Starvic et al	1980	38%	25%
2	Braun and Silver et al	1984	37%	29%
3	Klemi PJ et al	1990	59%	13%
4	Sclabas et al	2003	82%	12%
5	Rajpurohit et al	2010	77%	8%
6	PRESENT SERIES	2013	79%	5%

Fig. 27. Incidence of malignant histological types from different series



ACCURACY RATE

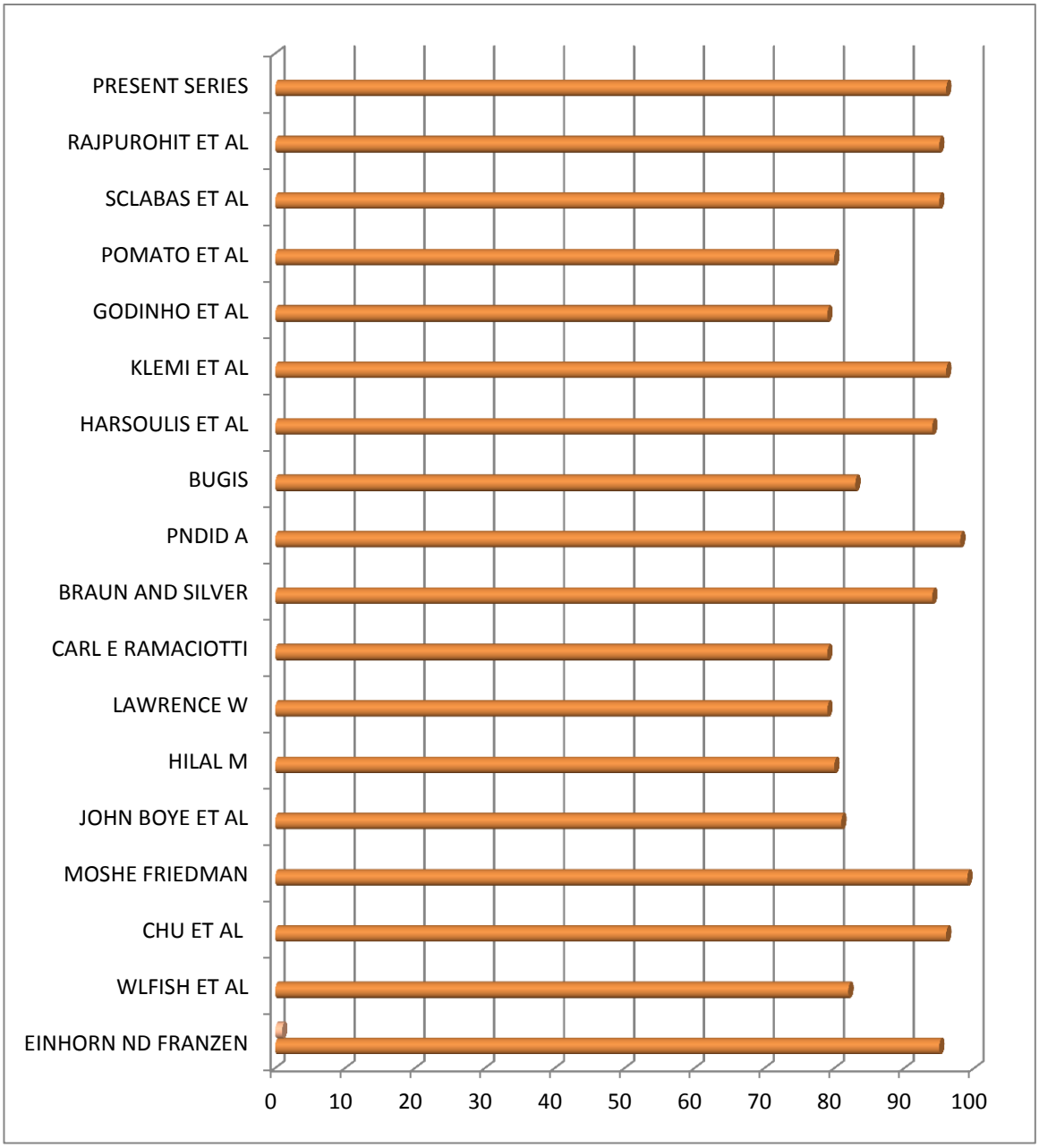
The overall accuracy was morethan 75% in the 15 series on the subject reported by various authors and morethan 90% in 7 series.

Fine Needle Aspiration of Thyroid Swellings : Overall Accuracy from different series

Table - 9

Sl.No.	Name of the Author	Year	No. of Cases	Total Accuracy	Percentage
1	Einhorn and Franzen	1962	216	205	95%
2	Walfish et al	1977	83	68	82%
3	Chu et al	1979	109	105	96%
4	Moshe Friedman	1979	244	242	99%
5	John Boye et al	1981	167	135	81%
6	Hilal M. Al Sayer et al	1982	50	40	80%
7	Lawrence W Morton et al	1982	225	178	79%
8	Carla E Ramaciotti	1984	119	94	79%
9	Braun and Silver	1984	65	61	94%
10	Pandid AA and Kinare SG	1986	43	42	98%
11	Bugis SP	1986	120	100	83%
12	Harsoulis et al	1986	190	179	94%
13	Klemi PJ et al	1990	198	186	96%
14	Godinho L et al	1992	28	22	79%
15	Pomato M et al	1997	85	68	80%
16	Sclabas GM et al	2003	240	228	95%
17	Rajpurohit et al	2010	130	124	95%
18	PRESENT SERIES	2013	100	96	96%

Fig. 28. FNAC OF THYROID SWELLING : OVERALL ACCURACY



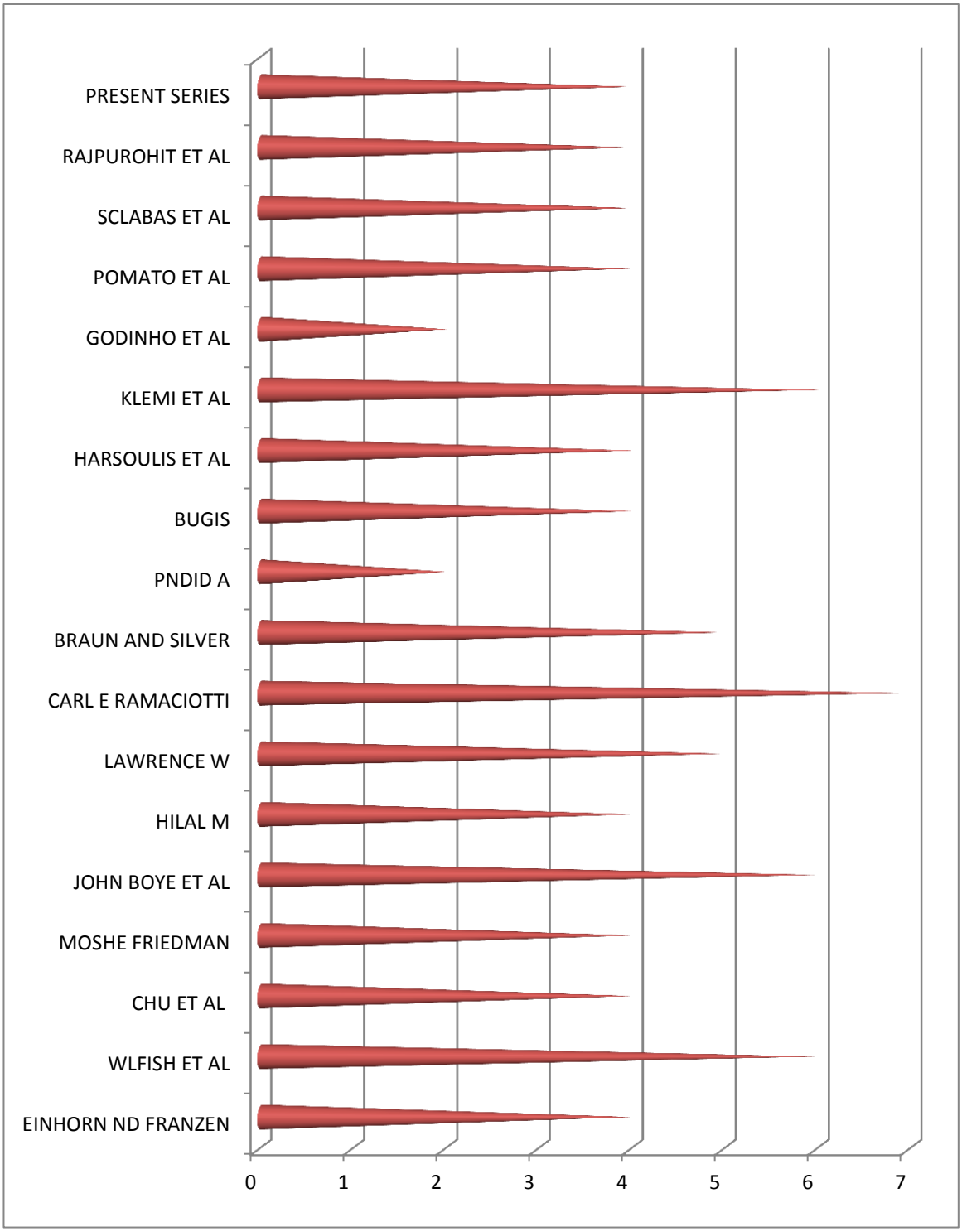
FINE NEEDLE ASPIRATION CYTOLOGY: FALSE NEGATIVE

FROM DIFFERENT SERIES

Table - 10

Sl.No.	Name of the Author	Year	No. of Cases	False negatives	Percentage
1	Einhorn and Franzen	1962	216	9	4
2	Walfish et al	1977	83	5	6
3	Chu et al	1979	109	4	4
4	Moshe Friedman	1979	244	9	4
5	John Boye et al	1981	167	10	6
6	Hilal M. Al Sayer et al	1982	50	2	4
7	Lawrence W Morton et al	1982	225	12	5
8	Carla E Ramaciotti	1984	119	8	7
9	Braun and Silver	1984	65	3	5
10	Pandid AA and Kinare SG	1986	43	1	2
11	Bugis SP	1986	120	5	4
12	Harsoulis et al	1986	190	7	4
13	Klemi PJ et al	1990	198	11	6
14	Godinho L et al	1992	28	1	4
15	Pomato M et al	1997	85	2	2
16	Sclabas GM et al	2003	240	9	4
17	Rajpurohit et al	2010	130	5	4
18	PRESENT SERIES	2013	100	4	4

Fig. 29 FNAC : FALSE NEGATIVE FROM DIFFERENT SERIES



FALSE NEGATIVES

The majority of false negatives were below 5 and in the present study the false negative was 4. The false negatives were due to misdiagnosis of papillary carcinoma as adenomatous hyperplasiaand nodular goiter and follicular carcinoma as follicular adenoma. The diagnosis of follicular carcinoma requires capsular and vascular invasion.The possibility of Papillary carcinoma with cystic degeneration must be kept in mind in cystic lesions though most of the lesions are benign, and wall must be aspirated after complete evacuation of the cyst. False negative results are uncommon, supporting the practice of observation in most of the patients.

PREDICTIVE VALUE

The predictive values of FNAC in the present series are :

SENSITIVITY	: 77.78%
SPECIFICITY	: 100%
POSITIVE PREDICTIVE VALUE	: 100%
NEGATIVE PREDICTIVE VALUE	: 95.35%
ACCURACY	: 96%.

SENSITIVITY AND SPECIFICITY

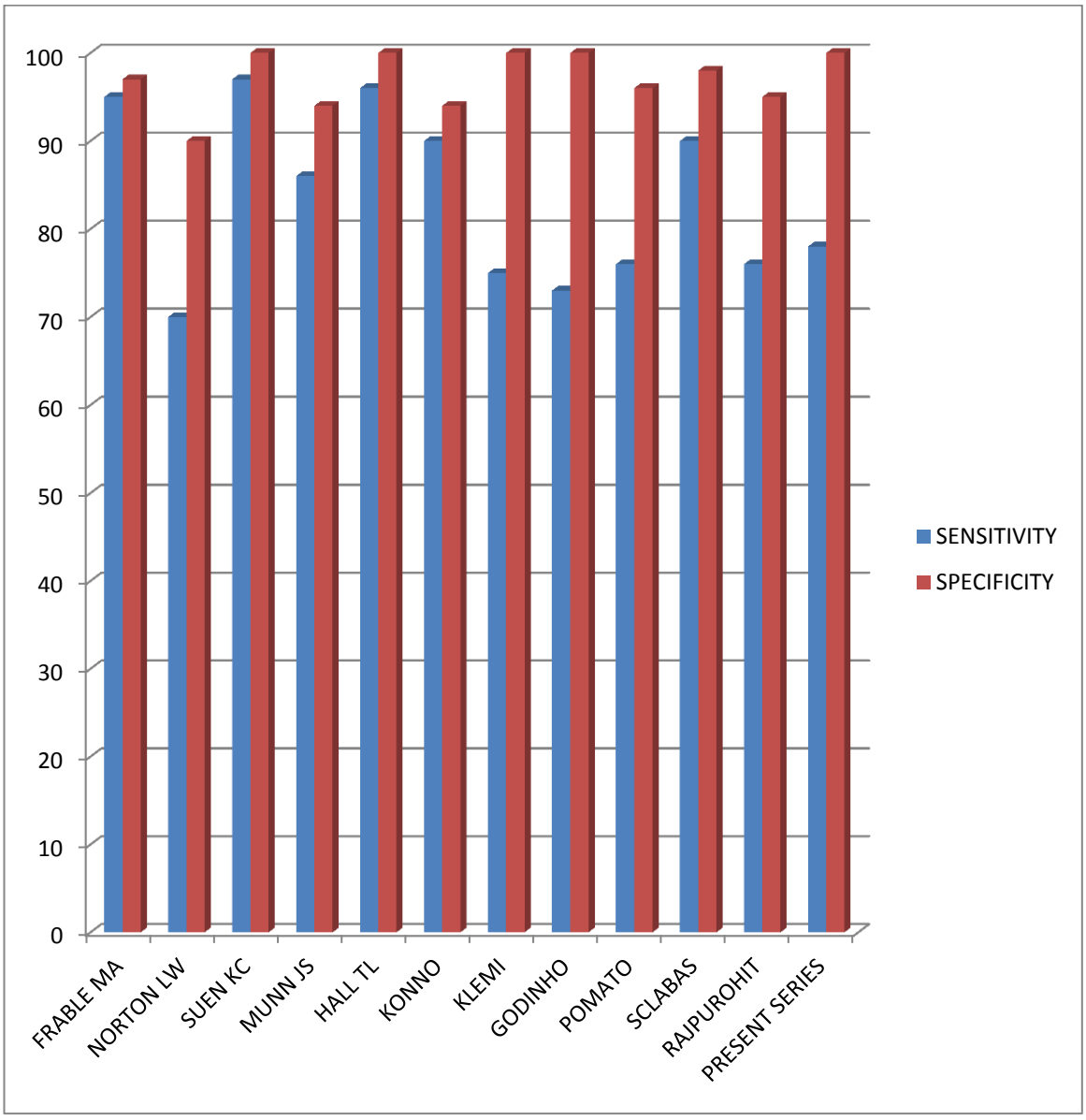
According to Frable MA (1980) the sensitivity and specificity of FNAC in thyroid diseases should be morethan 83%. Sensitivity and specificity from 8 different series showed to range from 70% to 100%. More false negatives decrease the sensitivity and specificity of the test.

FNAC OF THYROID LESIONS : COMPARISON OF SENSITIVITY AND SPECIFICITY FROM DIFFERENT SERIES

Table - 11

Sl.No.	Name of the author	Year	Sensitivity	Specificity
1	Frable MA	1980	95%	97%
2	Norton LW et al	1982	70%	90%
3	Suen KC et al	1983	97%	100%
4	Munn JS et al	1988	86%	94%
5	Hall TL et al	1989	96%	100%
6	Konno et al	1989	90%	94%
7	Klemi PJ et al	1990	75%	100%
8	Godinho L et al	1992	73%	100%
9	Pomato et al	1997	76%	96%
10	Sclabas et al	2003	90%	98%
11	Rajpurohit et al	2010	76%	95%
12	PRESENT SERIES	2013	78%	100%

Fig. 30 FNAC OF THYROID LESIONS : COMPARISON OF SENSITIITY AND SPECIFICITY FROM DIFFERENT SERIES



According to Suen KC and Queville NF (1983), a large cyst that reaccumulates haemorrhagic fluid after complete evacuation should be suspected for malignancy. Cytological diagnosis is less accurate for cystic than solid lesions(Walfish et al , Suen KC and Queville).

After studying the results of both FNAC and Core Needle Biopsy, Miller M et al and Colacchio et al (1979), concluded that the accuracy is similar but the superiority of FNAC lies in its simplicity and absence of complications. The accuracy does not exceed 90% with Vilms- Silermann needle, and the procedure is painful and traumatic and the specimen obtained is less representative. Complications like hemorrhage, hematoma and tumor implantation along the needle track have been reported. The procedure is useful for lesions less than 1.5 cm in size and in cystic swellings.

Among the large number for benign thyroid nodules occurring in the general population, detection of a malignant tumor is difficult and unreliable. Sophisticated investigations like ultrasonography, thyroid scintigraphy and biochemical tests are of little avail in resolving this diagnostic enigma. In Sweden FNAC has been used as a diagnostic modality in thyroid diseases for morethan 40 yrs, and over the last two decades it has gained popularity world wide. It has been used as first choice investigation for a solitary nodule thyroid. The method is cost effective and eliminates the need for diagnostic surgery. FNAC can also diagnose the underlying thyroiditis in a case of hypo or hyperthyroidism. Since the regular use of FNAC, unnecessary operations

on thyroid have reduced,cancer yield has increased and medical expenses and bed occupancy has decresed (Hamberger B et al,1982). Diagnosis from FNAC is very closely approximate to that on surgical biopsy (Miller M et al ,1979).

Pomato et al (1997) concluded that FNAC is certainly main diagnostic tool in diagnosing thyroid pathology. Its employment should undergo to a centralized diagnostic evaluation in such a way that cytology is analysed together with clinical and other instrumental data.

In a study conducted by Boeving, Anke, Cubas, Santos et lal (2005), they concluded that FNAC was accurate in the diagnosis of nodular thyroid disease, presenting a high correlation rate with histology.

In most of the cases, mistakes were because of

1. Confusion between nodular colloid or hyperplastic nodular goiter and Hashimotos thyroiditis, especially with Hurtle cell neoplasm. Orrel has quoted it as one of the difficulties in interpretation in 4 – 6 % of cases.
2. Difficulty in distinguishing multinodular goiter from follicular neoplasm.

CONCLUSION

1. MAJORITY OF PATIENTS WERE IN THE SEOND AND THIRD DECADES OF LIFE, FEMALES BEING PREDOMONANT.
2. MAJORITY OF CASES WERE BENIGN, OF WHICH MULTINODULAR GOITER (30.48%) WAS THE MOST COMMON PATHOLOGY.
3. AMONG THE MALIGNANCIES, MAJORITY WAS PAPILLARY CARCINOMA (79%).
4. THE SENSITIVITY,SPECIFICITY,NEGATIVE AND POSITIE PREDICTIVE VALUES WERE 77.78%,100%,95.35% AND 100%.
5. THE OVERALL ACCURACY WAS 96%.
6. FNAC WAS OF GREATER HELP IN THE DIAGNOSIS OF THYROID SWELLINGS. MULTINODULAR GOITRES AND COLLOID GOITRES WERE DIAGNOSED EASILY WITH FNAC,BUT CONFUSION PREVAILED IN CASES OF FOLLICULAR ADENOMA.
7. MAJORITY OF OUR CASES WERE RURAL FOLKS, WHO CANNOT BE FOLLOWED UP REGULARLY AND FOR LONG TIME, HENCE CLINICAL SUSPICION OF MALIGNANCY SHOULD BE ONE OF THE INDICATIONS OF SURGERY,INSPITE OF NEGATIVE FNAC REPORTS.

8. FNAC IS SIMPLER, SAFER, QUICKER AND MORE INFORMATIVE, COMPARED TO OTHER SOFISTICATED INVESTIGATIONS IN DIAGNOSIS OF THYROID DISEASES. IT SHOULD BE EXPLOITED TO ITS MAXIMUM BENEFIT ON ALL THYROID SWELLINGS.

SUMMARY

100 patients were studied from January 2012 to June 2013.

The histological diagnosis was compared with the cytological diagnosis in these cases.

Majority of thyroid cases (56%) were in the 2nd and 3rddecades of life (21-40) yrs, 88 were females and 12 were males,

Females : Males = 7.3 : 1

Among the 86 cases diagnosed cytologically as benign, 82 were proven histologically as benign. Of the remaining 4 cases,3 turned out to be papillary carcinoma and one as follicular carcinoma. The accuracy of FNAC in diagnosing benign lesions is 95.35%.

The predictive values of FNAC in the present series are :

SENSITIVITY	: 77.78%
SPECIFICITY	: 100%
POSITIVE PREDICTIVE VALUE	: 100%
NEGATIVE PREDICTIVE VALUE	: 95.35%
OVERALL ACCURACY	: 96%.

LIMITATIONS OF STUDY

The study sample selected is not a representative of the general population. Therefore the true incidence of various thyroid pathologies couldnot be assessed.

Some investigations which could have been useful, wasnot done due to lack of facilities.

The number of malignant cases studied during this limited period was not sufficient enough to make concrete conclusions, as regard to the sensitivity,specificity and accuracy of fine needle aspiration cytology of the malignant thyroid swellings.

Though our quantum of work is comparable with the standards, the experience of the cytopathologist could affect the study.

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PROFORMA

Name :

Age : Sex : IP.No. :

History :

Clinical Findings :

Thyroid function tests :

USG :

Clinical diagnosis :

FNAC No :

FNAC Report :

Surgery :

Gross findings :

HPE Report :

CONSENT FORM

ஒப்புதல் படிவம்

எனக்கு தைராய்டு சுரபியில் கட்டி உள்ளது. அதில் ஊசி போட்டு பரிசோதன செய்ய வேண்டும் என்பதை அறிகிறேன். பரிசோதனையின் போது இரத்த போக்கு ஏற்படலாம். பரிசோதனையின் முடிவு சரிவர வராவிடின் மறு பரிசோதனை செய்ய வேண்டியும் வரலாம் என்பதையறிந்து பரிசோதனைக்கு முழு மனதுடன் சம்மதிக்கிறேன்.

STATISTICAL METHODS APPLIED

The following statistical methods were applied in the present study

1. Cross tabs procedure
2. Descriptive stastistics
3. Sensitivity
4. Specificity
5. Positive predictive value
6. Negative predictive alue
7. Accuracy

Cross tabs Procedure

The cross tabs procedure forms two way and multi way tables and provides a ariety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine whaat test or measure to use.

Cross tabs statistics and measures of association are computed for two way tables only.

Descriptive statistics

This provides summary, information about the distribution, variability and central tendency of a variable.

Sensitivity

It is computed as follows$$\text{Sensitivity} = \frac{TP \times 100}{TP + FN}$$

Specificity

It is computed as follows$$\text{Specificity} = \frac{TN \times 100}{TN + FP}$$

Positive predictive value

It is computed as followsPositive predictive

$$\text{value} = \frac{TP \times 100}{TP + FP}$$

Negative predictive value

It is computed as follows Negative predictive

$$\text{value} = \frac{TN \times 100}{TN + FN}$$

Accuracy

It is computed as follows

$$\text{ACCURACY} = \frac{TP + TN \times 100}{TP + TN + FP + FN}$$

Where TP,TN,FP and FN imply True Positive, True Negative, False Positive and False Negative respectively.

KEY TO MASTER CHART

AC	-	Anaplastic carcinoma
C/O	-	Presenting complaints
CG	-	Colloid goiter
F	-	Female
FA	-	Follicular adenoma
FC	-	Follicular carcinoma
FN	-	Follicular neoplasm
FNAC	-	Fine needle spiration cytology
HCA	-	Hurtle cell adenoma
HPE	-	Histopathological examination
HT	-	Hashimotos thyroiditis
IP NO.	-	Inpatient number
HMT	-	Hemi thyroidectomy
M	-	Male
m	-	month
MFA	-	Microfollicular denoma
MNG	-	Multi nodular goiter
PC	-	Papillary carcinoma
RHT	-	Right hemithyroiodectomy
SL.NO.	-	Serial number
SNT	-	Solitary nodular goiter

STT	-	Subtotal tyroidectomy
SW	-	Swelling
TT	-	Total thyroidectomy
Yr	-	Year

MASTER CHART

Sl.No	Name	Age (yrs)	Sex	IP no.	C/O	Duration	Clinical diagnosis	FNAC	Surgery	Biopsy No.	HPE
1	Krishnammal	51	F	53080	SW	6m	SNT	AH	HMT	2524/12	FA
2	Kodiroja	52	F	52011	SW	5Yr	MNG	AH	STT	2527/12	MFA
3	Mallika	32	F	53253	SW	4Yr	MNG	HT	TT	2531/12	FA
4	Mariammal	35	F	52832	SW	2Yr	SNT	CG	HMT	2539/12	CG
5	sivagami	30	F	51328	SW	1yr	SNT	CG	HMT	2545/12	MFA
6	Pappa	48	F	54115	SW	6m	SNT	CG	HMT	2561/12	CG
7	ulagammal	42	F	51815	SW	3yr	MNG	AH	TT	2562/12	MNG
8	Tamaraiselvi	25	F	50775	SW	5m	SNT	AH	HMT	2600/12	FA
9	Chinnathai	40	F	53235	SW	4Yr	MNG	AH	TT	2602/12	MNG
10	Muthaal	54	F	54378	SW	4Yr	MNG	FN	TT	2622/12	MNG
11	Ganesh	28	M	55451	SW	2Yr	MNG	HT	TT	2643/12	HT
12	Gandhimathi	55	F	51978	SW	4Yr	MNG	AH	TT	2664/12	MNG
13	Abukasim	65	M	55495	SW	3Yr	MNG	CG	TT	2669/12	MNG
14	Regivamary	39	F	53251	SW	1Yr	MNG	PC	TT	2702/12	PC
15	Udayanagiri	28	F	56289	SW	3Yr	MNG	AH	TT	2705/12	MNG
16	Maliammal	27	F	56106	SW	6m	MNG	CG	TT	2711/12	CG
17	Venketalakshmi	47	F	57137	SW	8m	SNT	CG	HMT	2724/12	CG
18	Lakshmi	55	F	55849	SW	5m	SNT	CG	HMT	2728/12	MNG
19	Padmavathy	45	F	57151	SW	9m	MNG	CG	TT	2730/12	MNG
20	Usha	26	F	56785	SW	2Yr	MNG	AH	TT	2739/12	MNG
21	Sasikala	19	F	57326	SW	5Yr	MNG	CG	STT	2746/12	MFA
22	Vijayalakshmi	29	F	60553	SW	2Yr	MNG	CG	TT	2908/12	MNG
23	Vadivu	55	F	60981	SW	3Yr	MNG	HT	TT	2938/12	HT
24	Gomathy	40	F	63592	SW	5m	MNG	AH	TT	3029/12	PC
25	Sumithra	23	F	638110	SW	1Yr	MNG	CG	TT	3030/12	MNG

26	Karupyee	37	F	64914	SW	7m	MNG	PC	TT	3096/12	PC
27	Sakthi	53	F	65266	SW	5m	MNG	PC	TT	3125/12	PC
28	Jeyanthi	38	F	65206	SW	2Yr	MNG	CG	TT	3126/`12	FA
29	Syed Ali Fathima	28	F	66404	SW	9m	MNG	CG	TT	3160/12	HT
30	Muthulakshmi	35	F	63872	SW	3Yr	MNG	CG	TT	3164/12	MNG
31	Palkani	38	F	66419	SW	10m	SNT	CG	HT	3204/12	MNG
32	Panjavarnam	38	F	66646	SW	8m	MNG	AH	TT	3206/12	MNG
33	Pattathal	35	F	67426	SW	4Yr	MNG	AH	TT	3231/12	HT
34	Kaliammal	65	F	66418	SW	1Yr	MNG	PC	TT	3233/12	PC
35	Vemboo	55	F	67979	SW	5Yr	MNG	NG	STT	3234/12	HT
36	Thangam	25	F	66360	SW	4Y	MNG	HT	STT	3394/12	HT
37	Mariappan	55	M	68304	SW	10m	MNG	PC	TT	3401/12	PC
38	Usha	23	F	68425	SW	2Yr	MNG	PC	TT	3508/12	PC
39	Petchiammal	39	F	67721	SW	5Yr	SNT	NG	HMT	3600/12	FA
40	Rani	37	F	69695	SW	3Yr	MNG	AH	STT	3606/12	FA
41	Peratchi	28	F	70004	SW	1Yr	SNT	AH	HMT	3615/12	FA
42	Somu	45	F	70301	SW	4Yr	MNG	CG	TT	3642/12	HT
43	Velammal	32	F	70909	SW	1Yr	MNG	AH	TT	3653/12	HT
44	Pandy	23	M	71250	SW	9m	MNG	PC	TT	3657/12	PC
45	Mercy	29	F	71445	SW	11m	SNT	AH	STT	3690/12	MFA
46	Banu	45	F	71226	SW	4Yr	MNG	CG	TT	3695/12	NG
47	Sreenivasan	53	M	71447	SW	2Yr	MNG	PC	TT	3706/12	PC
48	Mariammal	40	F	71103	SW	7m	SNT	HT	HMT	3798/12	HT
49	Periyaswamy	32	M	71108	SW	9m	MNG	CG	TT	3999/12	CG
50	Chandra	45	F	74448	SW	5Yr	MNG	HT	TT	4128/12	HT
51	Akhila	15	F	74082	SW	4Yr	SNT	CG	HMT	4155/12	CG
52	Muthulakshmi	35	F	75852	SW	6Yr	MNG	AH	TT	4297/12	FA
53	Kanimmal	35	F	76402	SW	2Yr	MNG	HT	TT	4419/12	HT
54	Sankarammal	61	F	78833	SW	11m	MNG	AH	STT	4421/12	MFA
55	Subbuthai	53	F	88106	SW	5Yr	MNG	MNG	STT	4428/12	PC

56	Pitchammal	23	F	88327	SW	1Yr	MNG	AH	TT	4447/12	FA
57	Usha	20	F	89804	SW	3Yr	MNG	FN	TT	4480/12	FA
58	Ananthammal	22	F	91122	SW	9m	MNG	PC	TT	5180/12	PC
59	Janathi Beevi	33	F	95329	SW	1Yr	SNT	HT	HMT	5668/12	HT
60	Jamila	37	F	113003	SW	8m	SNT	CG	HMT	5699/12	MNG
61	Porkodi	30	F	113410	SW	1Yr	SNT	HT	HMT	5702/12	HT
62	Saraswathy	35	F	114197	SW	5Yr	MNG	PC	STT	5717/12	PC
63	Kala	22	F	112784	SW	4Yr	MNG	AH	TT	5718/12	MNG
64	Rathimuthu	45	F	115003	SW	2Yr	MNG	HT	TT	5734/12	HT
65	Kala	36	F	114345	SW	5Yr	MNG	HT	STT	5735/12	HT
66	Petchiammal	45	F	114427	SW	2Yr	MNG	HT	TT	5784/12	HT
67	Kaliammal	35	F	116611	SW	5Yr	MNG	AH	TT	5795/12	PC
68	Subbhulakshmi	33	F	117529	SW	4Yr	MNG	HT	TT	5818/12	HT
69	Subhuthai	49	F	118932	SW	1Yr	SNT	AH	HMT	5820/12	FA
70	Ponirulappan	24	M	119342	SW	5Yr	MNG	AH	TT	5868/12	MNG
71	Santha	34	F	134	SW	1Yr	SNT	CG	HMT	82/13	MNG
72	Esakiammal	17	F	194	SW	11m	SNT	CG	HMT	97/13	CG
73	Kathirel	62	M	206	SW	8m	SNT	FN	TT	99/13	MNG
74	Ramya	28	F	461	SW	3Yr	MNG	HT	TT	178/13	HT
75	Annathai	50	F	573	SW	9m	SNT	CG	HMT	198/13	MNG
76	Ponlakshmi	50	F	608	SW	3Yr	MNG	CG	TT	245/13	MFA
77	Vanapetchi	42	F	695	SW	4Yr	MNG	AH	TT	311/13	MNG
78	Chinnammal	40	F	801	SW	5Yr	MNG	FA	TT	389/13	FA
79	Balakrishnan	17	M	814	SW	2Yr	SNT	CG	HT	435/13	CG
80	Saraswathi	40	F	906	SW	4Yr	MNG	CG	TT	506/13	MNG
81	Sivanammal	65	F	1030	SW	1Yr	MNG	AH	TT	594/13	MNG
82	Anthonyammal	35	F	1235	SW	5Yr	MNG	CG	TT	696/13	MNG
83	Aanidaiammal	30	F	1429	SW	8m	SNT	HT	HMT	998/13	MNG
84	Noorjahan	60	F	1543	SW	4Yr	MNG	CG	TT	1002/13	MNG
85	Jessi	55	F	1558	SW	2Yr	MNG	HT	TT	1003/13	HT
86	Mydeen Beevi	33	F	1977	SW	5Yr	MNG	HT	TT	1010/13	HT

87	Solaiammal	22	F	1904	SW	1Yr	SNT	HCN	TT	1018/13	HCA
88	Esakkiammal	40	F	2332	SW	2Yr	MNG	CG	TT	1066/13	MNG
89	Resvammal	35	F	3093	SW	11m	SNT	AH	HMT	1088/13	MFA
90	Gomathi	75	F	3202	SW	2Yr	MNG	PC	TT	1106/13	PC
91	Anthonyraj	12	M	3314	SW	4Yr	MNG	HT	TT	1173/13	HT
92	Mahula	14	F	3476	SW	3Yr	SNT	HT	HMT	1208/13	HT
93	Lakshmi	33	F	3561	SW	2Yr	MNG	PC	TT	1224/13	PC
94	Shagunthala	55	F	3665	SW	1Yr	MNG	MC	TT	1247/13	MC
95	Kanagammal	24	F	3790	SW	4Yr	MNG	CG	TT	1254/13	CG
96	Muppidathi	33	F	4076	SW	3Yr	MNG	AH	TT	1299/13	MNG
97	Mokkammal	39	F	4988	SW	5Yr	MNG	HT	TT	1303/13	HT
98	Krishnan	53	M	5662	SW	1Yr	MNG	PC	TT	1307/13	AC
99	Mokkar	45	M	6154	SW	4Yr	MNG	HT	STT	1311/13	HT
100	Esakkiammal	44	F	6232	SW	2Yr	MNG	FA	TT	1414/13	FC